Virtual Reality in Pediatric Gait Rehabilitation

Thesis

presented to the Faculty of Arts

of the University of Zurich

for the degree of Doctor of Philosophy

by

Karin Birrer

Citizen of Kilchberg ZH

Accepted in the Spring Semester 2010

on the recommendation of

Prof. Dr. rer. nat. Lutz Jäncke

Prof. Dr-Ing. Robert Riener

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That the environment and our activities influence our lives is basic human knowledge; what is new is that we are starting to understand a little of how it happens.

(Johansson, 2004)

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In conclusion, this thesis was only possible with the collaboration of a lot of people from different institutes: from the Department of Neuropsychology of the University of Zurich, the Rehabilitation Center of the University Children's Hospital Zurich, the Sensory-Motor-Systems (SMS) Lab of the ETH Zurich and the Hocoma AG.

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Summary

In the context of rehabilitation task-specificity, repetition and intensity of training seem to be key factors in motor (re)learning and inducing neuroplastic processes in the brain. For this reason, the driven gait orthosis (DGO) Lokomat® has been considered an excellent therapy device since it intensifies locomotor training by increasing the amount of stepping practice per training session and decreasing the therapist's manual assistance. However, in spite of the device's positive effects, children in particular show little motivation towards the training process in a repetitive robot-assisted gait training (RAGT), because this training is rather monotonous and provides little incentives to continue for longer time periods. With the establishment of the Lokomat® in the field of gait rehabilitation, there has been an increased demand for interactive virtual reality (VR) games to promote higher participation and compliance. It has been shown that VR has the capability to create a rehabilitation environment in which the intensity of practice and feedback can be systematically manipulated to provide the most appropriate, individualized real-life motor training. However, so far only a few studies have focused on the efficacy of VR-based training conditions in gait rehabilitation of children.

Therefore, the main goal of this thesis is to investigate whether VR-based training scenarios enhance motivation and performance during RAGT in children. On the one hand, the VR-based scenarios implemented should engage children to such an extent that therapies may be applied on consecutive days for over 3-5 weeks and on the other hand, the output variables should reflect a patient's activity and thus provide motor feedback for both therapists and patients.

For this reason, in a first step various VR-based scenarios during RAGT have been tested in a single-case design to assess user acceptance and feasibility. With the most engaging VR-based scenario, we were able to show that the presence of a visual stimulus produced higher participation in one patient compared to the absence of such an incentive (chapter 6.1: Feasibility Study). In the first study (chapter 6.2), the immediate effect of different supportive conditions (VR versus non-VR) on motor performance was explored in children with neurological gait disorders and healthy controls during training with the Lokomat®. With regard to training efficiency, the VR-based scenarios used in this study had an immediate effect on motor output, which was similar to that effect resulting from therapist support. As a follow-up, the second study (chapter 6.3) investigated the

induction and maintenance of active participation on various forms of training interventions during RAGT. VR-based therapy approaches were most effective in inducing the desired participation in all children compared with other supporting training conditions. In the third study (chapter 6.4), additional advantages of VR games (i.e. supplementary movement patterns) were analyzed with the goal to determine changes in stance phase activity of the supporting leg performing a VR soccer kick during the Lokomat® training.

In conclusion, this dissertation supports the hypothesis that the VR scenarios implemented for RAGT have the capability to increase active participation and provide a appealing rehabilitation environment for children. Furthermore, it provides insightful information regarding active performance and motivation in children during Lokomat® training, thus broadening the range of studies in the field of VR-based gait rehabilitation.

Zusammenfassung

In der Rehabilitation spielen Faktoren wie aufgabenspezifisches Lernen, Repetition mit Variation und Trainingsintensität für das motorische Lernen eine wichtige Rolle. Dadurch können neuroplastische Vorgänge unterstützt und verlorene oder noch nicht entwickelte Fähigkeiten und Funktionen wie die Gehfähigkeit können wieder erlangt werden. Die Roboter-unterstützte Gangorthese Lokomat® hat sich als hervorragendes Therapiegerät erwiesen, da es ein intensives, automatisiertes Training erlaubt, welches einerseits die Schrittanzahl während einer Trainingseinheit erhöht und im Gegensatz dazu die körperliche Belastung der Therapeuten reduziert. Trotz diesen positiven Auswirkungen, zeigen gerade Kinder wenig Motivation was den Trainingsprozess eines roboter-unterstützten Gangtrainings (RAGT) angeht, da ein intensives und repetitives Üben oft mit Eintönigkeit und wenig Anreizen einhergeht. Mit der Etablierung des Lokomaten® im Bereich der Gangrehabilitation zeigte sich eine erhöhte Nachfrage für interaktive, auf virtueller Realität (VR)-basierende Spiele, um eine höhere Partizipation und Compliance zu erreichen. Es konnte gezeigt werden, dass VR die Fähigkeit hat eine Umgebung zu kreieren, wo die Trainingsintensität und das Feedback systematisch manipuliert werden können, um ein möglichst individuelles und angepasstes praxisnahes motorisches Training zu ermöglichen. Dennoch gibt es bis zum jetzigen Zeitpunkt nur einige wenige Studien, welche die Effizienz von VR-basierten Trainingsbedingungen in der Gangrehabilitation von Kindern untersucht haben.

Das Hauptziel dieser Arbeit besteht deshalb darin zu untersuchen, ob ein auf VR-basiertes RAGT die Motivation und Leistung bei Kindern erhöhen kann. Auf der einen Seite, sollen die implementierten VR-basierten Spiele die Kinder so begeistern, dass Therapien an mehreren aufeinanderfolgenden Tagen für ca. 30 Minuten über einen Zeitraum von 3-5 Wochen Spass machen. Auf der anderen Seite, sollen die Variablen, welche von den VR-basierten Spiele gewonnen werden können, die Partizipation des Patienten widerspiegeln und motorisches Feedback für Patienten und Therapeuten ermöglichen.

Aus diesem Grund wurden, in einem ersten Schritt, verschiedene VR-basierte Spiele während eines RAGT in einer Einzelfallstudie bezüglich ihrer Benutzerakzeptanz und Durchführbarkeit getestet. Mit dem vielversprechendsten und motivierendsten VR-Spiel konnte gezeigt werden, dass die Anwesenheit im Vergleich zur Abwesenheit von visuellen Anreizen eine höhere Partizipation bei einem Patienten hervorruft (Kapitel 6.1:

Feasibility Study). In der ersten Studie (Kapitel 6.2) wurde die unmittelbare Auswirkung verschiedener motivierender Bedingungen (VR im Vergleich zu ohne VR) auf die motorische Leistung bei Kindern mit zentralen Gangstörungen und gesunden Kontrollkindern während eines Lokomat® Trainings untersucht. Bezüglich der Trainingsleistung konnte gezeigt werden, dass das VR-basierte Spiel eine unmittelbare Auswirkung auf die motorische Leistung bei den Kindern hatte, welche vergleichbar waren mit den Auswirkungen durch therapeutische Unterstützung. In der Nachfolgestudie (Kapitel 6.3) wurde die Beeinflussung und Aufrechterhaltung der aktiven Teilnahme bei verschiedenen Formen von Trainingsinterventionen während eines Lokomat® Trainings untersucht. Bei allen untersuchten Kindern waren VR-basierte Trainingsansätze die effektivsten Trainingsinterventionen bezüglich der Beeinflussung der gewünschten Partizipation im Vergleich zu anderen (Nicht-VR) unterstützenden Trainingsbedingungen. Die dritte Studie (Kapitel 6.4) analysierte mögliche zusätzliche Vorteile von VR Spielen (z.B. zusätzliche Bewegungsmuster) mittels dem Vergleich der Standphasenaktivität des Standbeines während eines virtuellen Fussballkicks auf dem Lokomat®.

Zusammenfassend unterstützt die vorliegende Dissertation die Hypothese, dass VR-basierte roboter-unterstützte Gangtraining die Fähigkeit haben die aktive Teilnahme zu erhöhen und ein ansprechendes, rehabilitatives Umfeld für Kinder bieten können. Weiter bietet diese Arbeit aufschlussreiche Informationen bezüglich Partizipation und Motivation bei Kindern während eines Lokomat® Trainings und erweitert so die aktuelle Literatur im Bereich der VR-basierten Gangrehabilitation.

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Abbreviations

ADL	Activities of Daily Living
BWSTT	Body weight supported treadmill training
CP	Cerebral Palsy
CIMT	Constrained-Induced Movement Therapy
DGO	Driven Gait Orthosis
ICF	International Classification of Functioning, Disability and Health
ICF-CY	International Classification of Functioning, Disability and Health for children and youth
IMI	Intrinsic Motivation Inventory
KP	Knowledge of Performance
KR	Knowledge of Results
GMFM	Gross Motor Function Measurement
GMFCS	Gross Motor Function Classification System
MS	Multiple Sclerosis
NIRS	Near-infrared Spectroscopy
PVQ	Pediatric Volition Questionnaire
RAGT	Robot-Assisted Gait Training
SCI	Spinal Cord Injury
SMC	Sensorimotor Cortex
TBI	Traumatic Brain Injury
VR	Virtual Reality
WHO	World Health Organization

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1 Introduction

The development of efficient and independent walking is an important therapeutic goal for many children with neurological disorders. Current theories of motor learning suggest that task-specificity and repetition can promote recovery of neural pathways but that rehabilitation treatment programs are often shorter and less intensive than required to obtain the most optimal therapeutic result. Consequently, there has been a growing interest in improving treadmill training, and over the past decade, robotic devices have become increasingly implemented in gait training for patients with neurological disorders.

In this thesis, robot-assisted gait training (RAGT) has been combined with newly developed virtual reality (VR) scenarios to provide a more challenging and motivational environment for children with central gait impairment during daily therapeutic routine. Therefore, this thesis has its focus on whether VR-based intervention enhances motivation and performance in RAGT for children.

The first two introductory chapters described more closely developmental brain plasticity and its relevance for gait rehabilitation. Furthermore, feedback and motor learning are introduced and the terminology of virtual reality and its implication for motivation in pediatric rehabilitation is shown. In chapter 4, the general aim and significances are presented. An introduction to the methods and apparatus used in the present thesis is given in chapter 5. In chapter 6, the empirical studies in the form of independent manuscripts are presented. Finally, this thesis closes with the general discussion, which includes a summary of the results of the empirical studies, potential shortcomings and an outlook for future work.

After all I would like to emphasize that this challenging project could only be realized due to the research collaborations of various institutes: the Department of Neuropsychology of the University of Zurich, the Sensory-Motor Systems Lab, ETH Zurich, the Rehabilitation Center Affoltern a. A. of the University Children's Hospital and Hocoma AG.

2 Gait Rehabilitation

The World Health Organization (WHO) has defined rehabilitation as a coordinated process which enhances activity and participation[1]. The WHO International Classification of Functioning, Disability and Health (ICF) provides a multi-dimensional framework for health and disability suited to the rehabilitation process. An ICF adaptation specially designed for children and youth (ICF-CY), have acknowledged the peculiar and dynamic nature of many aspects of functioning in children and adolescents[1]. The overall domains in ICF not only focus body structure and function, but also on activity and participation from both the individual and societal perspectives. One major aim of rehabilitation therapy is to make qualitative and quantitative improvements in daily activities, thus improving the quality of independent living[2]. Since walking capacity has been identified by stroke patients as one of their most important goals, recovery and improvement of gait are central aspects of rehabilitation[3-5]. In accordance with basic principles of rehabilitation, active rather than passive patient participation is desired throughout the entire course of therapy[6].

2.1 Patient Population with Neurological Disorders

The Rehabilitation Center of the University Children's Hospital Zurich in Affoltern am Albis, Switzerland conducts automated gait training for children with gait impairments due to spinal or cerebral motor disorders. Therefore, children with various diagnoses, such as cerebral palsy (CP), stroke, traumatic brain injury (TBI), spinal cord injuries (SCI) or multiple sclerosis (MS), have been included for study. However, only the most common diagnosis for children treated at the Rehabilitation Center Affoltern a. A. have been described below:

CP, with an incidence of 2-3 per 1000 live births in Europe, is the most common motor disorder in children[7]. Although there have been several attempts in the past decade to define CP, it is currently defined as a group of non-progressive, permanent disorders which affect movement and posture that are attributed to disturbances occurring in the developing fetal or infant brain[8]. The motor disorders of CP are often accompanied by disturbances of sensation, cognition, communication, perception, behavior, and/or a seizure disorder. Gait limitations in children with CP are common and a prevalent functional outcome of therapy is the attainment of upright locomotion (i.e. walking)[9].

2.2 Plasticity in the Developing Brain

In the last twenty years, researchers have shown that developmental changes of the human brain occur from early childhood to adulthood. However, plasticity mechanisms are enhanced in the developing brain such that children can recover more fully from brain injuries than adults[10]. The term brain plasticity refers to how neuronal circuits can be modified by experience, learning and in response to brain lesions[11-13]. Due to the enormous amount of life-long training, professional musicians have shown to be an ideal model to investigate training-induced neuroplasticity and have set the stage for further research (for review see[14, 15]). Therefore, the concept of neuroplasticity and corresponding findings from those basic researches are of enormous relevance in the rehabilitation setting.

Given the degree of walking impairments often caused by neurological disorders such as stroke, TBI, SCI or CP, one major aim of rehabilitation is the restoration of such elementary capabilities to a normal level of performance. Regaining walking capacity was identified by stroke patients as one of the most important goals of rehabilitation[3-5]. In general, the recovery of motor functions after neural injury or disease depends on a variety of factors, including the nature and quantity of rehabilitation efforts[16, 17]. It is a common clinical observation that functional recovery often occurs following an injury such as stroke, although the extent of recovery is highly variable. Some patients may eventually achieve full recovery, while others have little or no improvements and remain severe impaired[18]. Previous work has been demonstrated that age influences recovery[19]. A recent review revealed that the developing human brain can compensate for acquired brain lesions more effectively than the adult brain[20]. Knowledge of the potential capability of the brain to compensate for lesions is a prerequisite for optimal rehabilitation strategies. However, the extent of compensatory processes is difficult to predict[12, 21].

Little is known about the neural mechanisms of locomotor recovery so far[22, 23]. This might be mainly due to technical limitations in assessing cerebral activation during dynamic movements. Miyai et al. (2001-2003) investigated human gait recovery after stroke using near-infrared spectroscopy (NIRS)[22, 24, 25]. They measured cortical activity during hemiparetic gait on the treadmill in 8 patients with initial stroke. Comparing cortical activation patterns during gait between healthy individuals and patients with stroke, one important difference is the asymmetry of activation[24]. Improvements of asymmetrical sensorimotor cortex (SMC) activation significantly correlated with improvement of gait parameters. These findings indicated that balanced SMC activation might play an important role in locomotor recovery after stroke[22]. Two other studies investigated VR rehabilitation intervention on cortical reorganization and associated locomotor recovery in a randomized trial with stroke patients[23] and in a case report of a child with cerebral palsy[26]. Results showed that cortical activation by the affected movement was reorganized from ipsilateral (before VR) to contralateral (after VR) activation in the laterality index and that this value after VR was comparable to the findings in normal individuals. Thus the authors concluded that VR may have contributed to the changes in neural organization and associated functional recovery[23].

However, further research is needed regarding restoration of gait in patients with neurological disorders. One possible key to increase motor recovery after neurological injury is task-specific training that induces activity-dependent plasticity. Researchers are developing new techniques in order to promote activity-dependent plasticity and maximal recovery and understanding brain plasticity provides a basis for developing better therapies to improve outcome of brain injuries[10]. Constraint-induced therapy and robot-assisted locomotor training are two of the new therapies that are demonstrating positive outcomes[27, 28].

2.3 Feedback and Motor Learning

The most fundamental principle in motor learning is that the degree of performance improvements is dependent on the amount of practice. Furthermore, neurorehabilitation often leads on the assumption that patients can improve with practice. Combining feedback with practice is considered to be a potent variable affecting motor skill learning[29, 30]. Feedback can be classified either as "intrinsic" (or task-intrinsic), which is the sensory-perceptual information when performing a skill or "augmented feedback" (extrinsic) and delivers additional information from an external source[31]. The external source may be a therapist or a device such as a biofeedback system or a computer. The augmented feedback is divided into either "knowledge of results" (KR) or "knowledge of performance" (KP). KR provides information about the outcome of the performance or about achieving the goal, while KP informs about the movement characteristics. Most often, KP is given by an external source observing the performance. Especially augmented feedback may have practical implications for rehabilitation therapy since the re-learning of motor skills is an important part of functional recovery[32-34]. But also, because patients abilities to generate intrinsic feedback may often be compromised or defect by neurological sensory impairments. Therefore, augmented feedback might be important for motor learning in the rehabilitation of patients with neurological disorders.

2.3.1 Biofeedback in Gait Rehabilitation

The term biofeedback refers to an augmented form of feedback. It provides information about physical processes like blood pressure, heart rate or muscle activity[31, 35]. Thus, augmented feedback delivers information about the success of a skill in progress. In the present work, biofeedback represents man-machine interaction forces and characterizes the degree of activity of the patient. In the method part, the description and measurement of the biofeedback is described in more detail.

2.4 Locomotor Training

Repetition and task completion appear to be dominant features of therapies and used to promote reorganization of neural pathways[36, 37]. New techniques that provide patients with functional exercise to promote activity-dependent plasticity and maximal recovery are of great importance. Previous observations made with the strategies of Constrained-Induced Movement Therapy (CIMT) and robot-assisted locomotor training have demonstrated positive outcomes in this direction[27, 28].

2.4.1 Manual Treadmill Training

Since walking is a highly repetitive human movement, locomotion therapy like manual assisted treadmill training and body weight supported treadmill training (BWSTT) has been well established in gait rehabilitation of patients with motor deficits[28, 38-41]. Although manual assisted gait training has been widely used and several studies endorse its effectiveness, there is little evidence concerning the effect of BWSTT on children[42, 43].

In spite of the fact that BWSTT can be initiated very early in the rehabilitation process, it has also several major limitations. For example, the duration of training sessions is usually limited due to personnel shortages and therapist fatigue. Furthermore, manual assisted training allows for neither repetition nor objective measurement of patient performance and progress[44-46]. This has led to the development of automated devices designed to increase the duration and quality of training[47, 48].

2.4.2 Robot-assisted Gait Training

Over the past decade, robotic devices have been implemented more and more frequently in gait training for patients with central gait impairment. As mentioned above, section, manually-assisted gait training has several shortcomings. In contrast, robotic devices provide an ideal initial position for objective, reproducible and continuous measurement of therapy[49]. Furthermore, RAGT have the advantage that number of training duration can be increased and sessions extended, while reducing the high level physical effort required for therapists. There are a number of robotic locomotor devices currently being used in rehabilitation research, including the electromechanical gait trainer, the Pelvic Assist Manipulator and the Lokomat®.

The most commonly used DGO Lokomat® can be adjusted according to force, speed and body weight support. It provides consistent assistance and can move the leg along a predefined fixed trajectory. However, one shortcoming is that the physical contact between the therapist and the patient is reduced, thus limiting opportunities for therapist feedback about patient's performance. Neither the patient nor the therapist is informed about the patient's muscle activity and performance. Therefore, since such feedback is essential for successful therapy, a quantification of the patient's activity was provided in the form of a computerized visual feedback[44, 45]. Man-machine interaction forces at hip and knee joint linear drives were measured and in order to estimate of the patient's level of contribution or performance. For a detailed description of the biofeedback measurement see chapter 5: Materials & Methods.

2.4.3 Clinical Feasibility and Effectiveness in Robot-assisted Gait Training

Although several studies have demonstrated improvements in locomotor ability in different patient population receiving RAGT[50-56], so far the literature appears to be controversial. The fact that there are only four randomized controlled-trials, which have investigated the effectiveness of RAGT points to the need for additional research in this area.

Husemann et al.[52] analyzed the effect of the Lokomat® training on 30 acute stroke survivors in a randomized controlled pilot study. In addition to 30 minutes of conventional physiotherapy training for each group, the treatment group received 30 minutes of robotic training daily and the control group 30 minutes of conventional physiotherapy daily. Results of the comparison of the effectiveness of Lokomat® training and conventional physiotherapy on gait rehabilitation showed that both groups experienced a significant and clinically meaningful increase in motor function. The fact that there was no difference between the groups in motor function before and after the treatment suggests that neither robot-controlled gait training nor regular physiotherapy has an advantage in terms of regaining gait function. However, the Lokomat® group displayed an advantage over conventional physiotherapy in improvement of gait abnormality and body tissue composition. Another blinded, randomized controlled study tested the feasibility and potential efficacy of using the DGO Lokomat® for treadmill training[51]. Sixteen stroke patients were randomly placed into two treatment groups, ABA or BAB (A = 3 weeks of Lokomat® training, B = 3 weeks of conventional physical therapy) for nine weeks of treatment. The more intensive and task-specific training provided by the Lokomat® led to several better walking outcomes (including speed, endurance, muscle strength and muscle tone) compared to the conventional phase of training. The authors concluded that despite the small number of patients, the present data suggested that the Lokomat® provides innovative possibilities for gait training. Schwartz et al.[57] reported similar results in another randomized controlled study. They investigated the effectiveness of early and prolonged locomotor treatment on the functional outcomes of patients after sub-acute stroke. Sixty-seven patients were randomly assigned to 2 groups: thirty-seven received RAGT and 30 were treated with regular physiotherapy. RAGT was administered 3 times a week for 30 minutes, combined with regular physiotherapy for 6 weeks. Control patients received the equivalent amount of regular physiotherapy. Patients in the RAGT group exhibited significant greater gains than the control group in their ability to walk independently. In summary, this study showed that RAGT combined with conventional physiotherapy produced promising effects on functional and motor outcome compared with regular physiotherapy alone after the end of a 6-week trial. In contrast to these promising results, Hidler et al.[58] showed opposite effects. This study consisting of a multicenter randomized clinical trial evaluated the efficacy of RAGT with conventional gait training in patients with sub-acute stroke. All 63 patients received twenty-four 1-hour sessions of either Lokomat® training or conventional gait training. The results indicated that the use of conventional rehabilitation strategies elicits greater improvements in overground walking speed and distance in individuals with moderate to severe gait impairments. All the reported randomized studies so far have focused on adult patients.

In the field of pediatric neurorehabilitation, there is a growing body of literature suggesting that RAGT is a feasible and safe treatment option for children with cerebral palsy with potential beneficial effects on standing and walking sections of the gross motor function measurement (GMFM) [54, 59, 60]. However so far there is only one randomized trial showed positive effects of RAGT compared to conventional therpy[61].

To summarize, training efficacy depends on a number of different parameters. Therefore, findings of RAGT need to be interpreted cautiously and examined in greater detail to fully exploit its beneficial effect, especially for pediatric patients. One possible explanation for the limited effectiveness of robotic devices might be the patient's passivity in the DGO Lokomat®. Studies have shown that active involvement in the production of a motor pattern resulted in greater motor learning and retention than passive movement[62-64]. Combining the advances of VR technology with RAGT might have a benefit for rehabilitation training.

Overall, the robotic device cannot replace conventional physical therapy but may serve as an adjunct therapy device, especially in the early stages following neurological disorders and in persistently poor walkers[51].

3 Virtual Reality for Gait Rehabilitation

3.1 Terminology of Virtual Reality

The successful integration of VR into multiple aspects of medicine, psychology and rehabilitation has demonstrated its potential benefits and advantages. The term *virtual reality* refers to an interactive, computer generated environment which simulates the real world. In other words, VR can be seen as an advanced form of human-machine interface which allows the user to interact with and become immersed in a computer-generated environment in a naturalistic manner[65, 66]. Three-dimensional interaction distinguishes a VR experience from watching a movie[65].

The benefits and advantages with the use of VR in rehabilitation are numerous. VR offers the capacity to individualize treatment needs while providing standardization of assessments and training protocol[2]. Moreover, the use of VR in rehabilitation therapy offers the physically disabled patients an opportunity to be active and independent in activities otherwise difficult to engage in or to perform training in a safe environment that resembles real life[67-69]. VR applications even open up the possibility for home-based rehabilitation. Especially, in the field of pediatric rehabilitation, the use of VR may be well suited for therapy with children as they often play and learn in interaction with computers and are open to new technology. In addition, almost everything a patient does in the virtual world can be captured, measured and stored for evaluation and research[68].

3.2 Virtual Reality for Neurorehabilitation

In recent years, the field of virtual reality (VR) has grown immensely. However, there are not many studies that investigated the effect of VR on therapeutic outcome in comparison to conventional training. So far VR applications were tested only in small patient groups and did not include control subjects. Nevertheless, preliminary results indicate that VR offers powerful options to provide therapy within a functional, purposeful and motivating context[2, 66]. The possibility to change the VR settings relatively easily, to grade task difficulty and to adapt it to individual patient capabilities are important advantages of VR, as these features are essential for cognitive and motor recovery. In neurorehabilitation there are a few key concepts which are affected by the advantages of the use of VR for motor learning, such as repetition, feedback and motivation[66]. As mentioned above, repetition is an important factor for motor learning and cortical reorganization. Additionally, feedback about performance is essential for successful learning and to practice movements over and over, participants must be motivated to endure tasks[66].

Two recent reviews concluded that the field of VR rehabilitation is still in an early phase of development and that the use of VR might be an effective treatment method for motor rehabilitation of children with specific disorders[68, 70]. However, the generalizability is restricted due to several methodological limitations such as small samples and the absence of control participants[68, 70]. Thus, further and more convincing research is needed.

3.3 Motivation in Children

Motivation is usually not a constant factor but a dynamic process that is dependent on many external and internal factors. In general, human behavior is influenced by individual intrinsic and extrinsic factors[71]. Intrinsic motivation is associated with individual interest and enjoyment in the task itself, whereas extrinsic motivation is based on external rewards or punishments. Brehm & Self (1989) defined potential motivation as created by needs and/or potential outcomes and the expectation that performance of a behavior will affect those needs and outcomes. The greater the potential motivation, the greater is the amount of energy that one will be willing to provide[72]. The Yerkes-Dodson law holds that performance is an inverted-U-shaped function of motivation. This law suggested that for an optimal performance, one needed to be optimally aroused whereas under-or over aroused leads to poor performance.

Several studies support the fact, that patients' motivation plays a crucial role in determining therapy outcome and that, in certain patient populations it may even be the most critical factor in defining the success of rehabilitation training (eg. in the field of pediatric rehabilitation)[17, 73-75]. Moreover it has been suggested that a more challenging and competitive situation as provided by virtual environments might increase patient's motivation to actively participate and thus shorten the time needed for motor skill recovery[17]. In the conceptual model of Bartlett and Palisano[76] was motivation the only child characteristic unrelated to health condition that was identified as a determinant of change in motor abilities in children with CP. Recently Majnemer et al.[77] described factors associated with motivation in children with CP. Children with CP had significantly lower motivation levels than typically developing peers. High motivation was related with fewer activity limitations, behavioral and family stress, whereas low motivation influences a child's full functional potential and effectiveness of interventions. Results also suggested that greater cognitive ability, better motor function and fewer functional limitations adhere with greater level of persistence in a specific task (i.e. motivation)[77].

Awareness of all the factors impinging on motivation for rehabilitation will also foster a better understanding of the phenomenon of patient disengagement in rehabilitation[78]. Rehabilitation training is indeed repetitive and repetition tends to "decouple" the mind and might reduce patient's motivation[79]. Similar in RAGT, where children have to complete standardized monotonous walking for 30-45 minutes per session, which is usually boring and can even be inconvenient. Hence, pediatric rehabilitation centers using RAGT try to boost patient motivation by showing DVDs or playing music. Such strategies, however, may distract children from the actual therapy, causing them to become completely passive and inattentive during the Lokomat® training. One solution might be VR technologies, which make it possible to directly interlink the patient's motor performance during the gait training with actions in a computer-game-like virtual world. Thus, VR games adequately adapted to children's needs provide motivation and yet keep the focus and attention on the actual gait training. Furthermore, VR techniques are adaptable to children's individual motor and cognitive skill level and adjust interactive elements to maximize motivation.

In this thesis, a greater level of participation during RAGT and children's reporting about their most enjoyable training intervention served as factors associated with higher motivation. However, one of the main challenges remains how to motivate children without biasing their reporting. In any event, motivation may be regarded as a booster during the process of pediatric rehabilitation.

4 Aims & Significance

The overall aim of the present thesis is to explore whether VR technology can be utilized as a training device in RAGT for children with neurological disorders. Thus, the focus is to investigate whether VR-based training scenarios enhance motivation and performance while training with the DGO Lokomat®. This was largely motivated by the need to develop engaging VR-based scenarios with the capability of creating a more appropriate rehabilitation environment for children. The previous chapters demonstrate that with the establishment of the Lokomat® in the field of pediatric gait rehabilitation, there is an increased need for interactive VR games to promote greater participation and compliance. So far, only a few studies have focused on the efficacy of VR-based training conditions in gait rehabilitation of children. It is of interest, therefore, to broaden current knowledge regarding the efficacy of VR-based scenarios on motivation and participation in children by investigating changes in motor output as reflected by man-machine interaction forces during RAGT.

Study 1 investigates which supportive conditions (VR versus non-VR) increase motivation and enhance motor performance during short Lokomat® training sequences. In this investigation, motor performance during various short conditions was assessed during training sessions using the Lokomat®. The motor output measured was quantified by a weighted sum of interaction forces between patient and the Lokomat® computed for each swing and stance phase for both hip and knee joints. Additionally, participants' acceptance of the Lokomat® training with VR was assessed using a self-designed motivation questionnaire for children. We hypothesize that the immediate motor output in all participants will be significantly higher for all participants during supportive conditions with VR compared to conditions without VR as a motivational factor.

Study 2 focuses on how well does the biofeedback correlates with an instructed level of activity in children. In addition, it examines how VR-based conditions influence motor performance and motivation during a longer Lokomat® training sequence in comparison with other supportive conditions. The first aim of this study assessed the validation of biofeedback values with instructed levels of activity. Based on the findings of study 1, the second study investigated two different VR conditions in longer training sequences with other supportive interventions. We assume that competitive situations (as in VR conditions) and augmented feedback serve as additional motivational factors and will thus lead to higher active participation and maintenance during conditions with VR compared to other conventional interventions without VR.

Finally, study 3 examines how stance phase activity of the supporting leg changes during a VR soccer kick in comparison with normal steps. In addition to the previously addressed effects of increased participation during VR conditions, this study assesses whether it is possible to train concurrently the supporting leg while concentrating on the kick during a VR soccer game. The impetus for this part of the study is to explore the changes in the stance phase activity during VR kick versus normal steps. Since patients tend to use their healthy leg favorably for a soccer kick during the VR-game, the objective of this study was to determine changes of the more affected supporting leg. Furthermore, we suggested that a prolongation of the stance phase during the kick would indicate that patients would more or less automatically train the weight bearing capacity of the supporting (more affected) leg.

5 Materials & Methods

5.1 Participants

A total of 46 participants were included in the different studies: 24 of them were patients with various types of central gait impairment and 22 were healthy children. For a detailed overview of participants included in the studies, see figure 1.

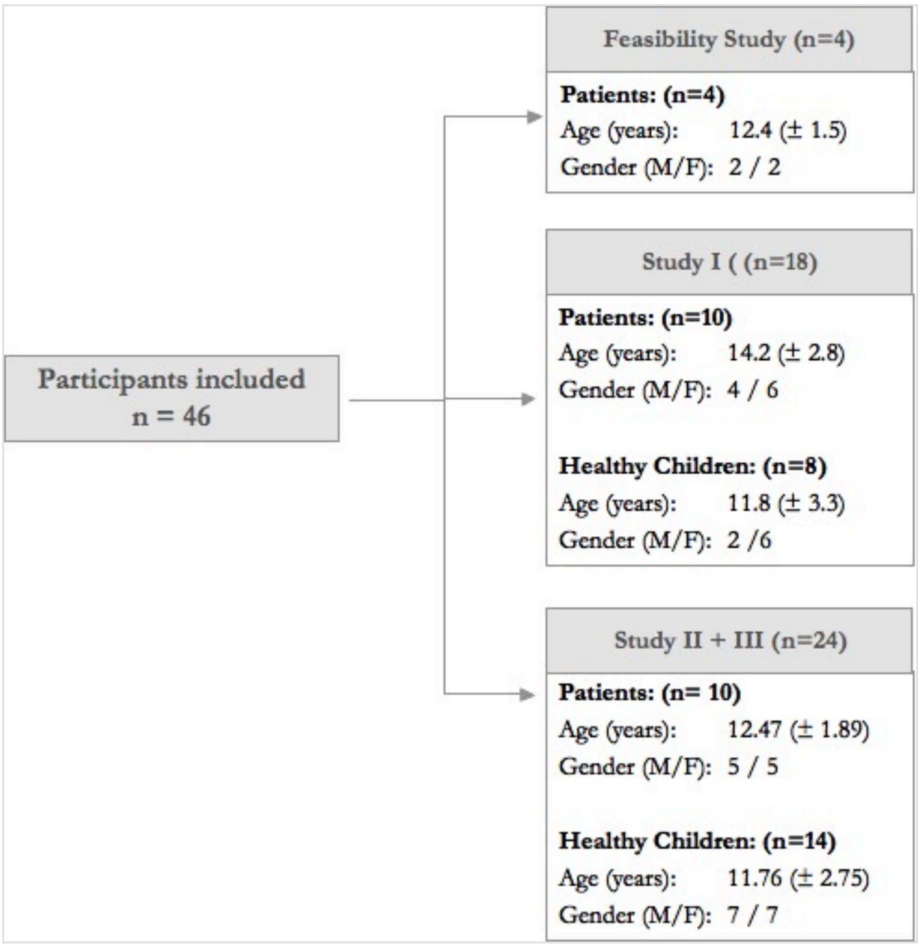

FIGURE 1: FLOW DIAGRAM OF THE PARTICIPANTS INCLUDED

5.2 The Driven Gait Orthosis Lokomat

The driven gait orthosis (DGO) Lokomat (Hocoma AG, Volketswil) was developed by researchers of the Spinal Cord Injury Center of the University Hospital Balgrist in Zurich and the Swiss Federal Institute of Technology (ETH), Switzerland. The Rehabilitation Center Affoltern am Albis of the University Children's Hospital Zurich has been involved in the development of a pediatric module of the DGO Lokomat and thus automated locomotor training in children with central gait impairment

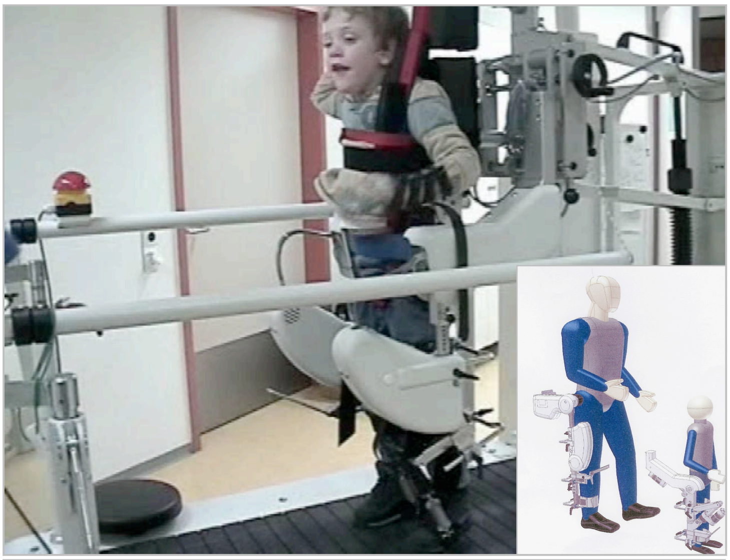

FIGURE 2: THE PEDIATRIC LOKOMAT AND A SCHEMATIC OVERVIEW OF THE TWO EXOSKELETONS (ADULT AND PEDIATRIC ORTHOSES).

due to either congenital (e.g. cerebral palsy) or acquired brain or spinal lesions can be offered[54]. The Lokomat consists of two actuated leg orthoses in combination with a body weight support system and a treadmill to control patient leg movements in the sagittal plane. The DGO is equipped with sensors at the hip and knee joint to measure man-machine interaction forces (figure 2). The legs of the patient are moved with highly repeatable pre-defined knee and hip joint trajectories on the basis of a position control strategy[46].

5.3 Biofeedback as Outcome Measure of Active Performance

The purpose of this biofeedback system was to assess activity and participation of subjects while training with the Lokomat gait orthosis. The biofeedback system was based on measured man-machine interaction forces in the hip and knee linear drives. These forces were processed in order to reward desired force production with positive biofeedback values and passive behavior with negative values. In order to obtain these positive and negative values, forces were multiplied by weighting functions for the hip and knee joints for each gait cycle and averaged for the stance and swing phase separately[44, 45].

The subject's legs are guided by the DGO with high impedance (equivalent to position control) along a fixed trajectory. With this high stiffness, changes in the subject's behavior are best detectable because already small deviations lead to large counteracting torques by the robot. The man-machine interaction forces of the drives give direct information about the patient's activity and performance. If a patient could perfectly match the movement of the device, the man-machine interaction forces would be zero[80]. If the patient is passive and does not contribute to the walking movement due to paresis or lack of motivation, the robot has to exert torque in order to move faster than the reference trajectory. Thus, the robot has to push the participant. Conversely, if the patient tries to move faster than the reference trajectory, the robot requires less torque or even has to decelerate the participant[44]. With this approach, the forces that the patient exerts onto the DGO are measured along each gait cycle and processed for each joint separately. This provided eight biofeedback values per step cycle (left and right hip and knee joint during stance and swing phase) to characterize the degree of activity of the patient[81].

5.4 Progress and Development of VR Scenarios

The requirements for VR-based RAGT have been defined in response to patient-specific deficits. Therefore, therapeutic training goals have been defined with respect to (a) increasing maximal force output of hip and knee flexors/extensors (b) adapting speed during walking (c) translating visual input into motor output (eye / limb coordination) and (d) initiating and terminating gait (figure 3).

	Soccer	Obstacle	Traffic	Water / Snow
Force		+		+
Range of Motion (ROM)	+	+		
Speed	+			
Coordination	+	+	+	
Cognition	+		+	

FIGURE 3: DEFINED THERAPEUTIC TRAINING GOALS WITH RESPECT TO VR SCENARIOS.

In the first feasibility study[82], we implemented four different training scenarios which addressed the aforementioned training goals. To strengthen their muscles and increase their range of motion, the participants waded through deep snow or kicked a soccer ball. In order to exercise the starting and stopping of walking movements and the change of walking speed, they were asked to walk through a street traffic scenario, i.e. crossing a street at a traffic light. Participant's gait-eye coordination and movement coordination were trained in the street traffic scenario and in an obstacle course (figure 4).

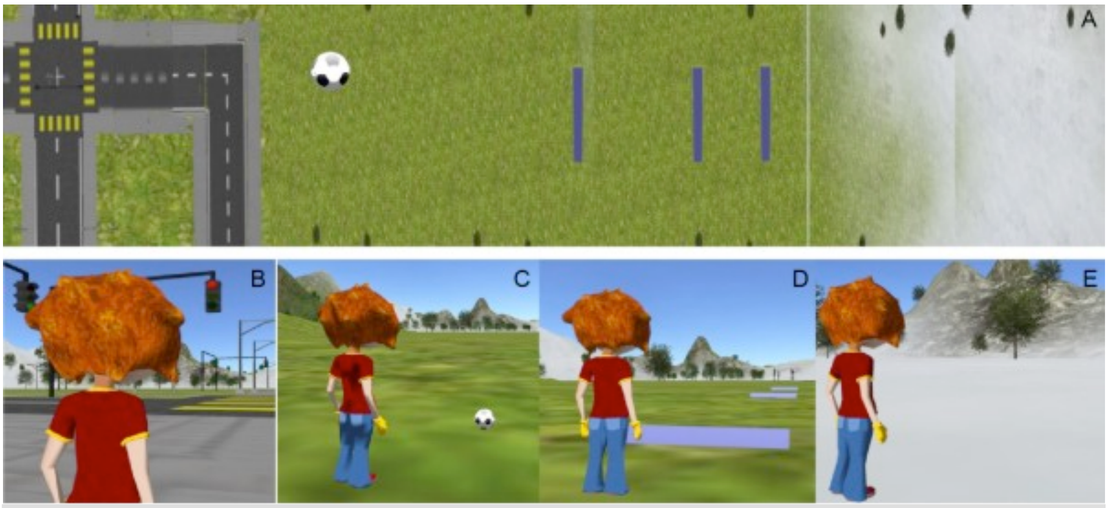

FIGURE 4: OVERVIEW OF THE FOUR VR GAIT COURSES (COURTESY: SMS, HOCOMA AG). (A) COURSE OF BIRD'S EYE VIEW OF ALL FOUR SCENARIOS. (B) AVATAR AT TRAFFIC LIGHT. (C) SOCCER SCENARIO. (D) OBSTACLE SCENARIO AND (E) AVATAR WADING TROUGH SNOW.

This feasibility study assessed levels of user acceptance for all four scenarios and identified the most engaging scenario: the soccer game. Therefore, the soccer scenario was continuously developed for the studies that followed.

The VR soccer game made it possible for participants to kick a ball in competition against two virtual opponents (figure 5A). Participants tried to kick the ball past the opponent directly in front of them. If they failed to do so, they had to start again from the last kick position. Should participants become too weak, the second opponent was configured to walk faster and take over the ball, should they participate actively again, the opponent would walk more slowly.

Another VR scenario, developed by Hocoma AG, was the navigation game used in study two of this thesis. This game used motivational incentives for participants engaged in collecting various objects (coins or treasure chests) or animals (figure 5B). The asymmetric physical activity of the legs induced turning in the virtual environment. To be specific, turning right and left could be induced by increasing activity of the contralateral leg of the desired direction, and decreasing activity of the ipsilateral leg, respectively.

FIGURE 5: VR SCENARIOS (A) VR SOCCER GAME WITH THE TWO OPPONENTS. (B) VR NAVIGATION GAME (COURTESY: SMS, HOCOMA AG).

A recent established cooperation with the Department Game Design of the "Zürcher Hochschule der Künste", Zurich has the purpose to develop new and suspenseful VR-based games for gait rehabilitation on the Lokomat. This collaboration called GABARELLO (Game Based Rehabilitation for Lokomat) was highly motivated by the need to keep children attentive and provide target specific rehabilitation with different performance levels during consecutive training sessions. The discipline of Serious Game Designs offers new possibilities of combining therapeutic aspects with challenging games and attractive graphics in order to achieve enhanced immersion of the patient[83].

5.5 The Virtual Environment System Setup

The VR setup was installed on the Lokomat, which consisted of a 42-inch flat screen and a 7.1 Dolby surround system. The graphic elements were programmed using the Ogre framework (http://www.ogre3d.org). The sound output was rendered using Fmod programmers API (http://www.fmod.org) and the graphics models were created in Maya (http://www.adobe.com). The Lokomat system was used as a multimodal feedback system: the input device translated the subject's movements into movements of an avatar in the virtual environment (VE). Furthermore, the Lokomat was able to display interactions with objects, such as a soccer ball, represented in the virtual environment with the purpose of providing haptic feedback to the participant. Koenig et al.[84] showed that the soccer simulation produces a physically realistic output force on ball contact.

5.6 Motivation Questionnaire

As mentioned above, motivation might be one of the most important factors in rehabilitation therapy. However, the assessment of motivation is most often approached on the basis of post-test questionnaires and rating scales specifically constructed to measure subjective motivation in a certain field. For several reasons, the assessment of motivation in the field of pediatric rehabilitation is not an easy task. First, there exist only a few motivation questionnaires which are developed for children. Second, children showed a tendency to social desirability when fulfilling questionnaires. Another factor might also be the different level of cognitive abilities in the children which participated in the study.

In the present thesis, motivation was assed by a self-designed motivation questionnaire which were based on the concept of the Intrinsic Motivation Inventory (IMI)[71], a multidimensional measure of subject's experience with regard to experimental task in adults and the Pediatric Volition Questionnaire (PVQ)[85, 86].

Therefore, participants' acceptance of Lokomat training with VR was assessed by a self-designed motivation questionnaire for children. We asked participants to rate the following points with regard to their experience with VR: their opinions about training with and without VR, the subjective value of the RAGT training in general and their effort during the VR training. The questionnaire was presented as a visual analogue scale (VAS).

6 Empirical Part

6.1 Conference Proceeding (Feasibility Study)

Virtual Environments Increase Participation of Children with Cerebral Palsy in Robot-Aided Treadmill Training

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Proceeding of "Virtual Rehabilitation 2008", Vancouver, British Columbia, Canada, pp. 121-126 (2008)

6.1.1 Abstract

Virtual environments can make repetitive motor rehabilitation exercises more motivating and thereby more effective. We hypothesize that participation-dependent multi-modal stimuli increase the patient's activity as expressed through force exertion during robot-aided treadmill training. In a single case study with one patient (12 years old), we were able to show that active participation increased in the presence of visual stimuli and decreased in their absence. For a feasibility study, we included four children with cerebral palsy in order to assess the user acceptance of four different virtual environment scenarios including a soccer scenario, a traffic situation, obstacle crossing and wading through deep snow. Using questionnaires, we found that only the soccer scenario provided sufficient interactive elements to engage the patients.

6.1.2 Introduction

Cerebral Palsy (CP) affects approximately 1.5 out of 1,000 children[87] and results in a wide variety of cognitive and motor impairments. Treadmill training is part of a rehabilitation program administered to CP patients in order to improve existing but limited walking capabilities[88]. The Lokomat gait orthosis was developed in the Spinal Cord Injury Center at the University Hospital Balgrist, Zurich, Switzerland, for the improvement and automation of neuro-rehabilitative treadmill training[47]. It consists of two actuated leg orthoses, which are strapped to the patient's legs. On each orthosis, two motors (one at the hip joint and one at the knee joint) guide the patient's legs on a physiological walking pattern. A pediatric version of the Lokomat has been recently developed and provides automated treadmill training for children aged four and up[54].

FIGURE 6: THE PEDIATRIC LOKOMAT (IMAGE COURTESY HOCOMA AG, VOLKETSWIL, SWITZERLAND)

Virtual environments (VE) in rehabilitation provide motivating training that can be superior to training in a real situation[2, 66]. It was shown that increased motivation[17, 89] and active participation[90] can lead to increased efficiency and advancements of motor learning in neuro-rehabilitation. Children in particular have little motivation towards the training process, as the training is too monotonous and lacks a stimulating entertainment. Enriched environments, highly functional and task-oriented practice environments were shown to be necessary for motor re-learning and recovery after stroke[90].

We hypothesize that patient participation as expressed through force exertion on the Lokomat during walking can be influenced by visual stimuli of a virtual environment. Our goal is individuated control over the visual stimuli: increasing participation as needed to maximize the success of rehabilitation, while appropriately decreasing participation before the patient becomes overstrained.

6.1.3 Methods

A. Virtual Environment System Setup

Therapeutic training goals for specific motor deficits of subjects with CP were identified to be (i) the increase of maximal force output of hip and knee flexors/extensors, (ii) speed adaptation during walking, (iii) translation of visual input into motor output (eye/limb coordination) and (iv) initiation and termination of gait.

We implemented a total of four training scenarios (Figure 7) that address the before mentioned training goals, including three with virtual ADL tasks and one non-ADL task. For strengthening muscles and increasing the range of motion, the patients wade through deep snow in a virtual environment or kick a virtual soccer ball. In order to exercise the starting and stopping of walking movements and the change of walking speed, the patients have to walk within a street traffic scenario, i.e. crossing a street at a traffic light. Patients exercise gait-eye coordination (translation of visual input into motor output) and leg motion coordination in the street traffic scenario and in an obstacle course. We described details of the scenarios in a previous paper[84].

The VE setup around the Lokomat Pro system (Hocoma AG, Volketswil, Switzerland) includes a 42-inch flat screen and a 7.1 Dolby surround sound system. The graphic elements are programmed using the Ogre framework (www.ogre3d.org), and the graphics models are created in Maya (www.adobe.com). The Fmod programmer API provides the framework for sound output (www.fmod.org).

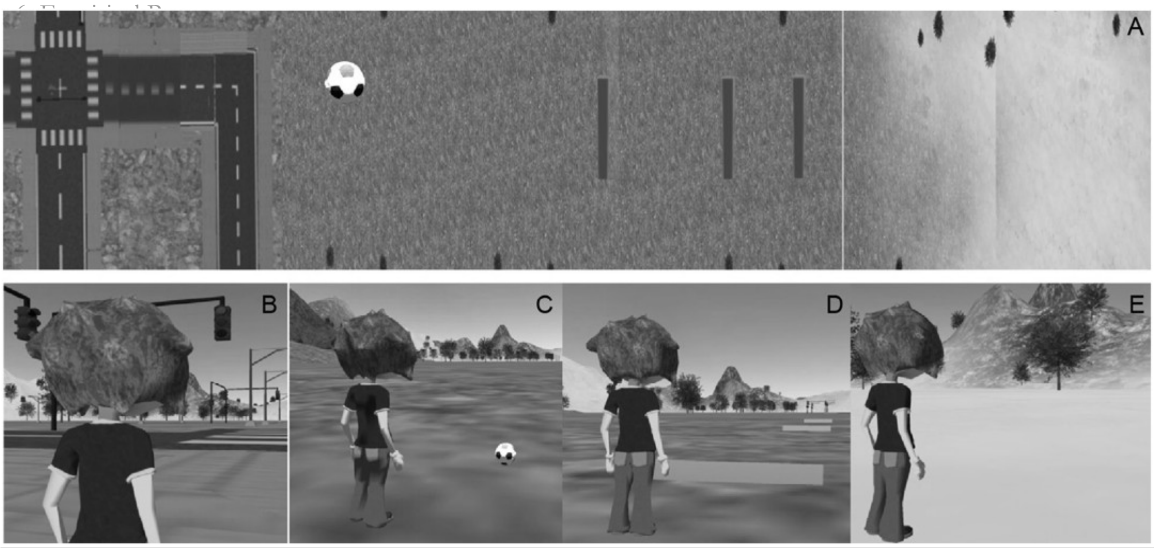

FIGURE 7: OVERVIEW OF THE VIRTUAL GAIT COURSE (COURTESY: SMS, HOCOMA AG.). (A) COURSE OF BIRD'S EYE VIEW OF ALL FOUR SCENARIOS. (B) AVATAR AT TRAFFIC LIGHT. (C) SOCCER SCENARIO. (D) OBSTACLES SCENARIO AND (E) AVATAR WALKING THROUGH SNOW.

The Lokomat is used as an input device of the patient's movements into the VE. An avatar in the VE mimics the movements of the patient. Additionally, it serves as a haptic display. Thereby force feedback of interactions of the virtual avatar with virtual objects is applied to the legs of the patient. The snow, the obstacle and the soccer scenarios include haptic interaction. Snow friction is implemented as a viscous friction force with quadratic velocity dependency. Coupling the lower leg's velocity with the friction force in the thigh produces the impression of snow friction. The haptic feedback of the obstacles is implemented as a spring damper system and includes a force feedback in normal and tangential direction. The soccer simulation produces a physically realistic output force on ball contact[84].

We provided three different modes of task difficulty from A to C depending on the severity of the disability. This makes the VE training challenging, yet feasible, for all patient groups. For clinical use in mode A, the Lokomat is position-controlled, actively moving the patient on the walking trajectory. To give the patient more control over the task, mode B provides 100% guidance force with the possibility of free movements during discrete events, e.g. for the swing leg during the kick of a soccer ball. Mode C employs a so-called path controller, giving the patient freedom in timing, whereas the robot merely ensures the spatial movement path and provides assistive force as necessary[91]. Each task has several levels of difficulty and employs some or all of the three modes. For the studies described in this paper, we only used modes A and B.

B. Biofeedback as Outcome Measures of Active Participation

Patient activity and participation during Lokomat training is quantified by weighted force measurements, the so-called biofeedback values[44]. The forces were measured in series with the spindle gear drives of the Lokomat (figure 8). The therapist cannot assess the activity level of the patient manually, because there is no physical interaction between the patient and the therapist in robotic automation gait training. The biofeedback values are weighted averages of the forces at the hip and knee joints, calculated for stance and swing phase. The weighting functions were defined for each part of the gait cycle, such that the resulting biofeedback values increase for therapeutically desirable movements, e.g. knee flexion for early swing.

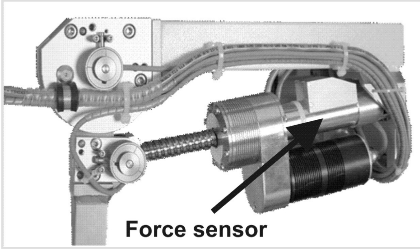

FIGURE 8: FORCE SENSOR ON THE RIGHT HIP JOINT OF THE LOKOMAT (IMAGE COURTESY OF HOCOMA AG, VOLKETSWIL, SWITZERLAND).

Force measurement F_i at time t_k, is weighted with $w_{i,j}$ and scaled with the offset $o_{i,j}$. Thereby$i \in [0, 1]$, with 0 being the hip joint and 1 the knee joint and $j \in [0, 1]$ where j=0 is the stance and j=1 the swing phase. Details of the computation and the weight functions can be found in[45]. The biofeedback values are unit less, positive when the patient is actively participating and negative when the Lokomat carries the burden of moving the patient. Comparing the biofeedback values of one subject over several Lokomat training sessions is tempting but not directly possible. Slightly altered attachment of the orthosis on the legs of the patients during the training session can lead to changes in the absolute values. The comparison between biofeedback values for training with and without VE as a measure of active participation is also difficult, as the patients without VE are typically motivated by the therapist. This is not the case for training with VE.

We implemented a virtual opponent in the soccer scenario that plays soccer against the patient (Figure 9A). The patient steers his avatar through the virtual environment. The opponent is configured to walk faster than the patient when the patient's biofeedback is low and slower when the patient participates actively. As an additional motivation factor, the opponent is able to take over the soccer ball from the avatar when he is ahead of the avatar. When walking behind the opponent, the avatar is able to catch up by actively participating and producing high biofeedback values. Whereas the position of the subject's avatar is computed as an integral over the walking speed, the position of the opponent in the virtual environment is calculated with an additional, biofeedback dependent speed adaptation factor Δv.

$$x_{Opponent} = \int \left(v_{tm} + \Delta v_{Opponent} + v_{Offset}\right) dt \qquad (1)$$

Where v_{tm} is the treadmill speed and

$$\Delta v_{Opponent} = G \cdot sig(\sum_{i=1}^{N} \frac{1}{N} BF_i), i \in [1,2,3,4] \qquad (2)$$

is a velocity offset set by the therapist. $BF_1 =$ biofeedback hip left, BF_1 =biofeedback knee left, BF_1 =biofeedback hip right, BF_1 =biofeedback knee right. The multiplier G scales the minimal and maximal deviation of the biofeedback dependent walking speed component. G=1 scales the maximal deviation $\Delta v_{Opponent}$to $\pm 1m/s$.

Within the VR, the camera is positioned 1.68 meters shifted slightly to the right behind the avatar (Figure 9B). When the opponent is more than 1.68m behind the avatar he is not visible on the screen.

We expect the visibility of the opponent to increase and the absence of the opponent to decrease active participation during Lokomat training. Compared to the pure display of numerical biofeedback feedback values, the opponent provides the possibility to produce a challenging situation on demand of the therapist.

We filtered the position data of the opponent with a low pass filter of 2Hz in order to eliminate noise that was inserted as an artifact of the recording procedure. 2 Hz appeared reasonable as the patient would not perceive and react to position changes of the avatar above this cut off frequency.

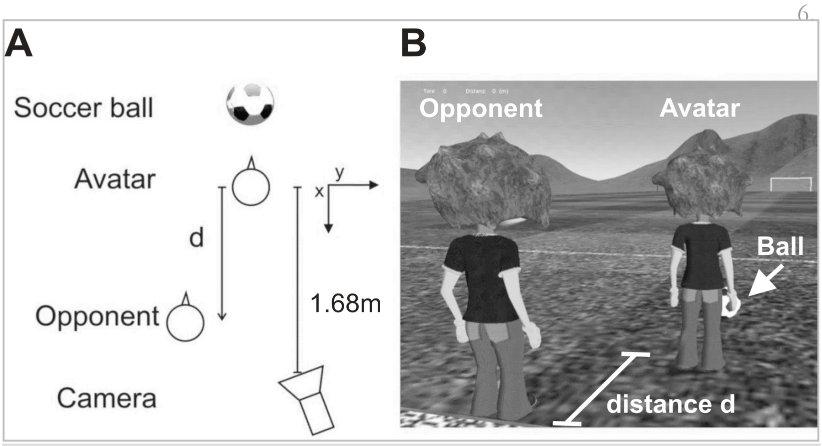

FIGURE 9: SOCCER GAME. (A) SCHEMATIC DRAWING OF THE RELATIONSHIP BETWEEN THE AVATAR AND THE OPPONENT. THE DISTANCE D BECOMES LARGER FOR INCREASING LEAD OF THE AVATAR OVER THE OPPONENT. WHEN THE OPPONENT IS CLOSER THAN 1.68M HE REACHES THE FIELD OF VIEW OF THE AVATAR. A NEGATIVE DISTANCE D IS EQUIVALENT TO A LEAD OF THE OPPONENT OVER THE AVATAR. (B)

C. Clinical Methods

We first performed a feasibility study to assess user acceptance for all four scenarios and to identify the most engaging scenario. The most engaging scenario was then used in a second study. In this second study, we investigated the influence of the VE onto the participation of patients.

Both studies were conducted at the rehabilitation center Affoltern am Albis of the University Children's Hospital Zurich, Switzerland. Approval for the studies was obtained from local ethics committees, and the legal guardians of all patients gave written informed consent. Patients were eligible for the study if they had central gait impairment due to either congenital or acquired brain or spinal lesions. Femur length had to be at least 21cm, which includes children from above four years. Further, patients had to be able to signal pain, fear or discomfort and had to be cooperative.

A total of four patients (Table 1) were included in the feasibility study to assess the developed VE-based technologies (mean age 12.4 years, std. 1.5 years). The aims of study were (a) to determine whether patients quickly learned to use the system in order to perform the four different scenarios, and (b) to assess the patient motivation for the four different scenarios.

TABLE 1: DESCRIPTION OF THE PATIENTS IN THE FEASIBILITY STUDY

Patient No.	Sex	Age (y;m)	Height (cm)	Diagnosis	Number of training sessions with VE	Mean training duration (min)	Mean walking distance (m)	Mean walking velocity (km/h)
1	F	10;4	138	BS-CP (III)[a]	13	26.22	693.85	1.64
2	F	12;11	154	BS-CP (II)	15	28.21	845	1.77
3	M	13;3	155	TBI [b]	5	25:07	722.60	1.74
4	M	12;4	150	MMC[c]	4	23:38	664	1.67

[a] bilateral spastic cerebral palsy with the Gross Motor Function Classification System level (GMFCS); [b]Traumatic brain injury; [c] spina bifida cystica (myelomeningocele)

We observed how the patients interacted in the virtual environment and evaluated the psychological effects of the scenarios (attention, concentration and motivation) by using motivational questionnaires (Pediatric Volitional Questionnaire PVQ)[86] for therapists and a self generated motivation questionnaire for children. We asked the participants to rate their experience in the VE concerning their interest in the scenario, their own perceived competence, the value of the VE training and their own effort during training (table 2).

TABLE 2: ANALYSIS OF QUESTIONNAIRES FOR FEASIBILITY STUDY

	Specific Question	Score (5= Yes, very much, 1= No, not at all)				Average
		Patient 1	Patient 2	Patient 3	Patient 4	
(1) Interest:	• Did you have fun to do the training?	5	4	4	3	**4**
	• Which scenario did you like most?	Obstacles	Soccer	Soccer	Soccer	**Soccer**
	• Do you look forward to the next training?	5	4	3	3	**3.75**
(2) Perceived Competence	• Do you think you did well at this training?	5	4	2	3	**3.5**
	• Dou you think you improved your training?	5	5	4	4	**4.5**
(3) Value / Usefulness	• Do you believe this training could be beneficial to you?	5	5	5	4	**4.75**
	• For what could this training be useful?	to walk without crutches	to walk better	to walk better	-	
(4) Effort	• How much effort did you put in the training today?	5	5	2	3	**3.75**
	• How important is it to you to do well at this activity?	5	4	4	3	**4**

The second study was performed with a twelve year old patient, diagnosed with bilateral spastic cerebral palsy, who had a Gross Motor Function Classification (GMFCS) level of three. The aim was to evaluate the influence of the VE on the participation of the patient. Based on questionnaire results of the feasibility study, we decided to perform further studies only on the soccer scenario, which the subjects of the feasibility study evaluated to be most motivating. The obstacle, snow and traffic scenarios in the current state of development were not sufficiently engaging, as they were not sufficiently interactive. The subject walked for several training sessions without VE and one session in the soccer scenario. The opponent was visible for the patient only after he approached the patient avatar with to a distance of approximately 1.68m (Figure 4). Within the soccer scenario, difficulty settings were: guidance force 100%, reduction in guidance force during soccer ball kicking: 95%, walking speed varied between 1.5 km/h and 2.3 km/h.

6.1.4 Results & Discussion

For the feasibility study, the questionnaire revealed that three of the four scenarios (traffic, snow, obstacle) lacked motivational and attention aspects. Three of the four patients judged the soccer scenario to be most engaging. One patient judged the obstacles and traffic scenario as most engaging. All verbalized the benefit of the Lokomat training as necessary to improve their walk. One patient accredited his newly acquired ability to walk without crutches to the VE based Lokomat training. Furthermore, all patients expressed their wish to use the VR system on an ongoing basis. All four expressed a desire for more interaction to influence the virtual environment.

We performed a second study on the influence on the participation of the most engaging VE scenario, which was identified to be the soccer scenario. This second study consisted of a 29-minute training session in the virtual soccer scenario walking against an opponent that could overtake the avatar and take away the soccer ball. Results of the second study show an increase of biofeedback values corresponds to an increase in active patient participation. This key definition was justified in the methods section. We compared biofeedback values depending on the distance of the opponent from the avatar. The minimal and maximal biofeedback values during the whole training duration were -22.9 and 235.0.

We found increased mean biofeedback values for the time the opponent was visible and decreased values when the opponent was not visible. Quantitative results are displayed in Table 3. For 77.2 percent of the training duration, a visible/non visible opponent coincided with above mean/below mean biofeedback values

TABLE 3: MEAN BIOFEEDBACK VALUES AND STANDARD DEVIATION FOR THE OVERALL BIOFEEDBACK

	Biofeedback	
	Mean	Std.
Total	55.8	52.4
Opponent visible (d<1.68m)	105.6	50.3
Opponent not visible (d>=1.68m)	33.7	35.4

Exemplary, Figure 10 shows a quantitative plot of the absence respectively presence of the opponent overlaid with the biofeedback plot.

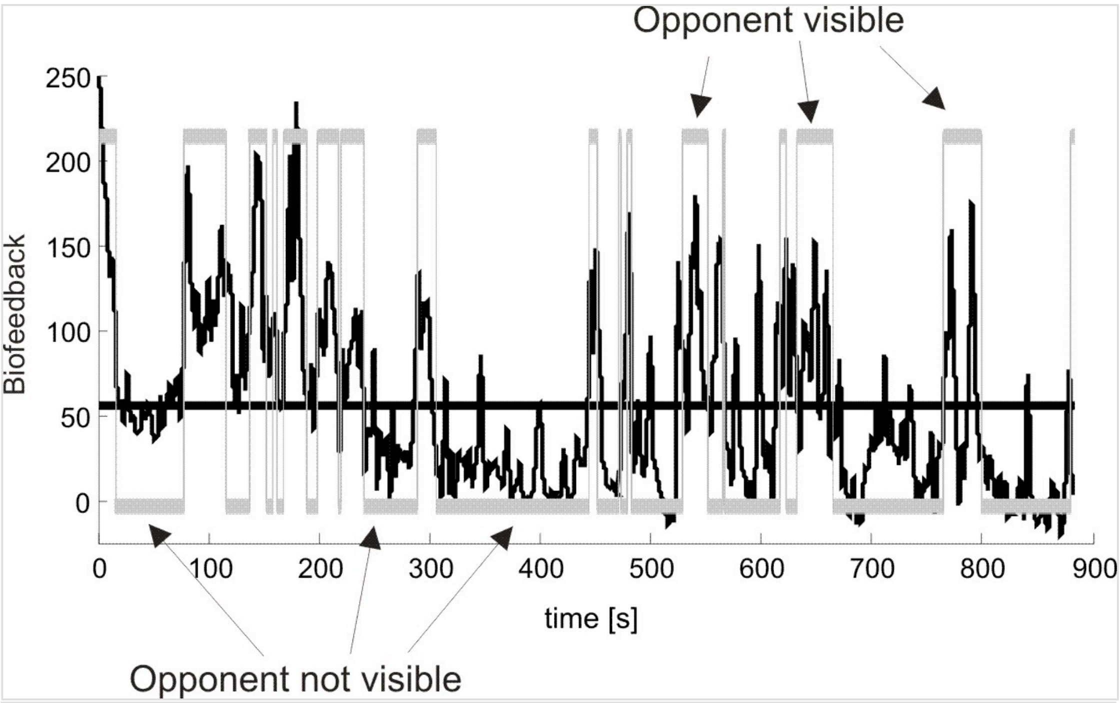

FIGURE 10: SUM OF THE BIOFEEDBACK VALUES DURING SWING PHASE OF BOTH HIP AND KNEE JOINTS FOR ONE TRAINING SESSION. THE MEAN BIOFEEDBACK VALUE IS 55.8. THE GRAY LINES INDICATES WHEN THE OPPONENT WAS VISIBLE OR NOT FROM THE PATIENT'S PERSPECTIVE.

For the time span [16; 77] or [305; 444] second, the distance d between opponent and avatar was larger than 1.68m, the opponent was not visible and the biofeedback at that time was below the mean biofeedback. Conversely, for time [632; 665] or [763; 799] seconds, the opponent position was visible with a maximal distance of 1.68m behind the avatar or even in front of the avatar. The biofeedback for these intervals increased over the mean biofeedback. During the training, the patient was able to keep the avatar for 25 minutes 13 seconds ahead of the opponent (87 percent of the total training duration) and kicked the soccer ball 35 times. The opponent took over the ball 5 times and kicked it.

6.1.5 Conclusion & Outlook

We were able to show that the presence of a virtual opponent in a VE produced higher participation of children with congenital or acquired gait impairment when compared to the absence of this visual stimulus. Future development of the scenarios must focus on the implementation of interactive, motivating elements. Further improvements in the soccer scenario are necessary to maintain high motivation during longer Lokomat trainings. The results of the single case study are part of the design process of the clinical study with control and intervention groups that will be performed in the future.

ACKNOWLEDGMENT

We want to thank the movement scientists and physiotherapy team for their cooperation and help during the measurements. We also thank the children, who participated in this study.

6.2 Publication: Study 1

Influence of Virtual Reality Soccer Game on Walking Performance in Robotic Assisted Gait Training for Children

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6.2.1 Abstract

Background: Virtual reality (VR) offers powerful therapy options within a functional, purposeful and motivating context. Several studies have shown that patients' motivation plays a crucial role in determining therapy outcome. However, few studies have demonstrated the potential of VR in pediatric rehabilitation. Therefore, we developed a VR-based soccer scenario, which provided interactive elements to engage patients during robotic assisted treadmill training (RAGT). The aim of this study was to compare the immediate effect of different supportive conditions (VR versus non-VR conditions) on motor output in patients and healthy control children during training with the driven gait orthosis Lokomat®.

Methods: A total of 18 children (ten patients with different neurological gait disorders, eight healthy controls) took part in this study. They were instructed to walk on the Lokomat in four different randomly-presented conditions: (1) walk normally without supporting assistance, (2) with therapists' instructions to promote active participation, (3) with VR as a motivating tool to walk actively and (4) with the VR tool combined with therapists' instructions. The Lokomat gait orthosis is equipped with sensors at hip and knee joint to measure man-machine interaction forces. Additionally, subjects' acceptance of the RAGT with VR was assessed using a questionnaire.

Results: The mixed ANOVA revealed significant main effects for the factor CONDITIONS ($p < 0.001$) and a significant interaction CONDITIONS x GROUP ($p = 0.01$). Tests of between-subjects effects showed no significant main effect for the GROUP ($p = 0.592$). Active participation in patients and control children increased significantly when supported and motivated either by therapists' instructions or by a VR scenario compared with the baseline measurement "normal walking" ($p < 0.001$).

Conclusions: The VR scenario used here induces an immediate effect on motor output to a similar degree as the effect resulting from verbal instructions by the therapists. Further research needs to focus on the implementation of interactive design elements, which keep motivation high across and beyond RAGT sessions, especially in pediatric rehabilitation.

6.2.2 Background

Given the degree of walking impairments often caused by neurological disorders such as stroke, traumatic brain injury, spinal cord injury or cerebral palsy (CP), one major aim of rehabilitation is the restoration of such elementary capabilities. Regaining walking capacity was identified by stroke patients as one of the most important goals of rehabilitation[3-5]. In general, the recovery of motor functions after neural injury or disease depends on a variety of factors, including the nature and quantity of rehabilitation efforts[16, 17]. However, conventional rehabilitative training programs are often shorter and less intensive than required to obtain an optimal therapeutic outcome. Nor do they adequately increase the patients' motivation or promote their active participation. Several studies support the fact that patients' motivation plays a crucial role in determining therapy outcome and that, in certain patient populations it may even be the most critical factor in defining the success of the rehabilitation training (e.g. in stroke patients)[17, 74, 75, 78]. Moreover, it has been suggested that a more challenging and competitive situation as provided by virtual environments might increase patient's motivation to actively participate and thus shorten the time needed for motor skill recovery[17]. Furthermore, it is believed that passive guidance is less effective for motor learning and restoration of walking compared to active performance[63, 92]. Preliminary results indicate that virtual reality (VR) offers powerful therapy options within a functional, purposeful and motivating context[2, 66]. Previous studies, especially in pediatric rehabilitation, have demonstrated the potential of VR with regard to various aspects (e.g. improvements of life skills, mobility, cognitive abilities, fun and motivation)[93-95]. Nevertheless, supportive evidence for the application of VR in the rehabilitation of children with neurological disorders is still poor since the research is dominated by uncontrolled trials with only a small number of cases and case series[68].

Robotic-based technologies for gait rehabilitation such as the driven gait orthosis Lokomat® (Hocoma AG, Volketswil, Switzerland) offer highly standardized, repetitive gait training, relieve the therapists' physical strain of manually guiding training and allow objective measurements of performance and progress. On the other hand, it is difficult to estimate a patient's performance during robotic assisted gait training (RAGT) due to the loss of physical contact between therapist and patient[44, 96]. Therefore, in RAGT it is essential that patients participate actively rather than just

FIGURE 11: ROBOTIC ASSISTED GAIT TRAINING (RAGT). CHILD ON THE PAEDIATRIC LOKOMAT WITH THE DISPLAY PRESENTED TO THE SUBJECTS DURING THE VR SOCCER

letting themselves "be walked". Combining the Lokomat with advanced VR technologies seems to be a promising option for rehabilitation therapy as it allows controlling and manipulating feedback parameters and thus leads to more challenging situations (Figure 11).

The present study was designed to systematically test the efficacy of combining the Lokomat with VR in children with central motor gait impairment and a healthy control group. We developed a motivational VR-based soccer scenario, which provides interactive elements to engage patients during RAGT. Children's level of activity and participation during RAGT were quantified by weighted force measurements output by the Lokomat - the so-called biofeedback values[44]. The biofeedback values are weighted averages of the forces at the hip and knee joints, calculated for the stance and swing phase. In RAGT training without VR, therapists typically try to motivate the patient maximally to obtain higher force output in hip and knee muscles, which serves as an important training goal. In VR, the virtual scenario is supposed to adopt, at least partially, the motivational role of therapists. Therefore, in the present study we compared the immediate effect of different supportive conditions (therapist's instruction versus VR-based scenario) on motor output (biofeedback values). We hypothesize that the immediate motor output in all participants will be significantly higher during supportive conditions with VR compared to conditions without VR as a motivational factor.

6.2.3 Methods

The study was approved by the local Ethics committee and brought into conformance with standards in the Declaration of Helsinki. Written informed consent was obtained from the legal guardians of all subjects before inclusion in the study. All measurements were conducted at the Rehabilitation Centre in Affoltern a. A. of the University Children's Hospital in Zurich, Switzerland.

6.2.3.1 Participants

Current as well as former patients with neurological gait disorders of the Rehabilitation Centre Affoltern a. A. of the University Hospital Zurich were screened for eligibility. A total of 18 children took part in this study: Ten patients (four males, six females, mean age 14.2 years, SD 2.8 years) with different neurological gait disorders and eight healthy children (two males, six females, mean age 11.8 years, SD 3.3 years). Patients had an average weight of 46kg (SD 12.1kg) and an average height of 157cm (SD 15cm). Healthy control children had an average weight of 41.7kg (SD 11.7kg) and an average height of 149cm (SD 13cm), which did not differ significantly from the patient group. Demographic characterization of the participants is given in Table 4.

Inclusion criteria for all participants were: (1) aged 4-18 with a femur length between 21 and 47cm (2) minimal voluntary control of their lower-extremity muscles to ensure that they had the ability to respond and adapt their walking and could follow different walking instructions (3) ability to signal pain, fear, discomfort and (4) willingness to meet the study requirements. One healthy control subject had to be excluded from the analysis due to data loss during recording.

TABLE 4: CHARACTERISTICS OF PARTICIPANTS WITH AND WITHOUT NEUROLOGICAL GAIT DISORDERS

Subject No.	Sex	Age (years)	Height (cm)	Weight (kg)	Lokomat's Legs K =kids T = Teens	Diagnosis (GMFCS-Level)
VP_01	f	10.3	140	44.3	K	-
VP_02	m	13.5	154	40	T	-
VP_03	f	12.1	148	40.8	T	CP, diplegia (II)
VP_04	f	11.3	140	32.8	K	-
VP_05	m	8.4	127	25.0	K	CP, diplegia (II)
VP_06	m	15.11	168	47.8	T	CP, diplegia, (II)
VP_07	f	16.10	178	60.8	T	Hip dysplasy
VP_08	f	9.3	137	32	K	-
VP_09	f	17.6	161	56.0	T	Cerebral hemorrhage
VP_10	f	15.4	168	50.1	T	Multiple Sclerosis
VP_11	f	10.10	140	34	K	-
VP_12	f	15.3	169	58.6	T	Encephalopathy
VP_13	m	16.8	158	46.7	T	CP, tetraplegia (III)
VP_14	m	8.11	143	33	K	-
VP_15	f	14.4	160	47.8	T	Symptomatic SCI
VP_16	f	17.2	168	53	T	-
VP_17	f	16.11	169	64.5	T	-
VP_18	m	13.1	139	27.0	K	CP, tetraplegia (II)

Abbreviations: CP=Cerebral Palsy; MS=Multiple Sclerosis; SCI=Spinal cord injury

6.2.3.2 Virtual Environment System Setup

The VR setup was installed on the Lokomat, which consisted of a 42-inch flat screen and a 7.1 Dolby surround system. The graphic elements were programmed using the Ogre framework (www.ogre3d.org). The sound output was rendered using the Fmod programmers API (www.fmod.org) and the graphics models were created in Maya (www.adobe.com). The Lokomat system was used as a multimodal feedback system: the input device translated the subject's movements into movements of an avatar in the virtual environment (VE). Furthermore, the Lokomat was able to display that interactions with objects, such as a soccer ball, represented in the virtual environment with the purpose of providing haptic feedback to the subject. Koenig et al.[97] showed that the soccer simulation produces a physically realistic output force on ball contact.

The Biofeedback of the Lokomat gait orthosis is based on the interaction torques between the subject and the orthosis. For this reason, the hip and knee linear drives are equipped with force sensors, which measures the force that is required to keep the subject on the predefined gait trajectory[96]. For clinical use, the Lokomat is normally position-controlled with 100% guidance force. Changes in the participant's behavior are best detectable during this high stiffness, because small deviations lead to large counteracting forces. Additionally, we provided the possibility of free movements during a discrete event, i.e. for the leg swing during the kick of a soccer ball.

FIGURE 12: OVERVIEW OF THE VR SOCCER SCENARIO. DISPLAYING THE VR SOCCER GAME WITH THE TWO OPPONENTS IN RED AND WHITE THE PATIENT (IMAGE COURTESY OF SMS, HOCOMA AG).

The soccer game made it possible for participants to kick a soccer ball in competition against two virtual opponents (Figure 12). One was waiting in front of the participant, who had to kick the ball past his opponent, otherwise he had to start from the last kick position. The second would approach from behind, taking over the soccer ball when he outpaced him. This second opponent was configured to walk faster and take over the ball from the participant if the exertion of the participant was weak and to walk slower when the subject participated actively. Within the VE, the position of the camera was slightly shifted to the right, providing an over-the-shoulder view. When the opponent was more than 1.68m behind the avatar, the opponent was not visible on the VR screen. In our previous study[82], we were able to show increased mean biofeedback values for the time when the opponent was visible and decreased values for the time the opponent was not visible. Therefore, we assume that a constant competitive situation could serve as an additional motivational factor. Hence, in the current soccer implementation, the therapist was able to manipulate the opponent's speed offset and walking according to the skills of a participant.

6.2.3.3 Procedures

Participants were instructed to walk on the Lokomat under four different randomly-presented conditions: (1) normal walking without supporting assistance from the therapist (BASELINE), (2) with therapists' standardized instructions to promote active participation (THER), (3) use of VR as a motivating tool to walk actively (VR), and (4) use of the VR tool combined with therapists' standardized instructions (VR + THER). The measured motor output was quantified by a weighted sum of interaction forces between patient and Lokomat which is computed for each swing and stance phase for both hip and knee joints[80]. The weighting functions were defined for each part of the gait cycle, such that the resulting biofeedback values increased for therapeutically desirable movements, e.g. knee flexion for early swing phase. All patients and

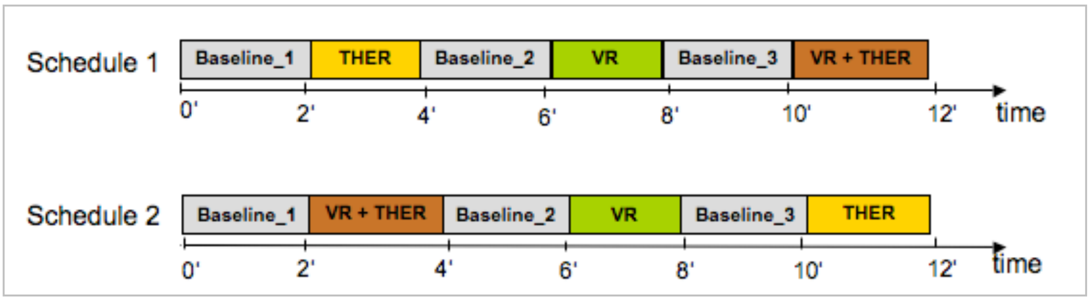

FIGURE 13: THE TWO DIFFERENT EXPERIMENTAL SCHEDULE STRUCTURES. SHOWING THE TWO DIFFERENT SCHEMATIC TIME SCHEDULES FOR THE PRESENTED STUDY WITH ALL CONDITIONS. THER: THERAPEUTIC INSTRUCTIOS. VR: VIRTUAL REALITY SOCCER SCENARIO. VR + THER: COMBINATION OF VR AND ADDITIONAL THERAPEUTIC INSTRUCTIONS.

participants were randomly assigned to two test schedules with balanced age distribution to avoid fatigue effect. After being fitted into the driven gait orthosis and before starting the first condition, children walked approximately five minutes in the Lokomat to familiarize themselves with the device. Each schedule began with and included in total three BASELINE measurements. Each walking condition lasted two minutes (Figure 13). During all conditions, children walked at their own comfortable speed (average for children's legs was 1.5km/h, for teenager's legs 1.7km/h) with 30% body weight support and foot-lifting straps, which assisted ankle dorsiflexion for adequate toe-clearance during the swing phase. All instructions given by the therapist were standardized for all conditions.

Participants' acceptance of the Lokomat training with VR was assessed by a self designed questionnaire for children. We asked the participants to rate the following points with regard to their experience with VR. their opinions about training with and without VR, the subjective value of the RAGT training in general and their own effort during the VR training. The questionnaire was presented as a visual analogue scale (VAS).

6.2.3.4 Statistical Analysis

We recorded the four biofeedback values (bilateral hip and knee joints) during all conditions for the swing-phase only, because Lünenburger et al.[44] demonstrated that there was a high correlation between only the swing phase and the instructed activity, whereas correlation involving the stance phase was low and sometimes even negative. The biofeedback values are unit less, positive when the patient is actively participating and negative when the Lokomat carries the load of moving the patient on its predefined joint trajectory. To describe the individual overall walking performance under each condition, the mean of all four biofeedback values was calculated for each step. Thereafter, the mean of all biofeedback values during one condition was calculated. This provided one biofeedback value for each condition (BASELINE, THER, VR, VR + THER).

First, all data were examined for normality. The statistical analysis for the three baseline measurements in all subjects was calculated using repeated measures ANOVA. Motor output parameters were analyzed using a 2 x 4 mixed ANOVA with GROUP (patient versus healthy controls) as between-subjects factor and CONDITION (BASELINE, THER, VR, VR+THER) as within-subjects factor. A post hoc analysis was performed using a paired t-test for comparisons between conditions. In general, effects were considered meaningful when they fell below $p < 0.05$. We performed post hoc analysis using Bonferroni-Holm corrected t-tests for paired samples, applying the correction procedure that Holm[98] suggested. This procedure refers to a step-down method on the basis of classical Bonferroni-Holm correction for multiple comparisons. In the present article, the largest p value is adjusted according to the number of all tests (N), whereas the second most extreme p value is adjusted according to (N-1) tests, and so on. T values were reported as being significant only if the corresponding p value survived the correction procedure characterized by the initial p value of .05 and the number of tests. Statistical analysis was performed using the statistical software package SPSS 16 for Mac, release 16.0.1 software (SPSS Inc. 2007, http://www.spss.com).

6.2.4 Results

The analysis of the three baseline (baseline_1, baseline_2, baseline_3) measurements revealed no significant main effect for the factor CONDITION ($F = 1.779$; $p = 0.186$) of the mean motor output. Therefore, the values for the three baseline conditions showed no fatigue effect and were allowed to be combined as mean total baseline.

The mixed ANOVA revealed significant main effects for the factor CONDITIONS $_{\text{(Baseline, VR, THER, VR+THER)}}$ ($F = 35{,}567$; $p < 0.001$) and significant interaction CONDITIONS $_{\text{(Baseline, VR, THER, VR+THER)}}$ x GROUP $_{\text{(patients, healthy controls)}}$ ($F = 4.268$; $p = 0.01$). Tests of between-subjects effects showed no significant main effect for the GROUP $_{\text{(patients, healthy controls)}}$ ($F = 0.3$; $p = 0.592$). Contrasts of within-subjects revealed significant effects for the

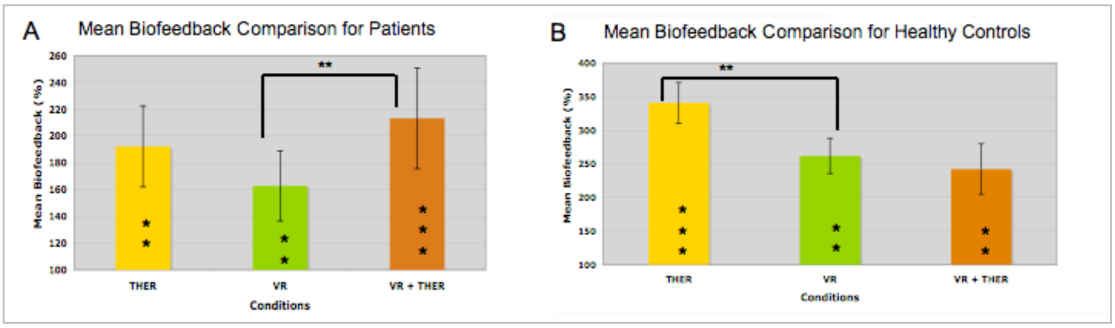

FIGURE 14: MEAN BIOFEEDBACK IMPROVEMENT FOR PATIENTS AND HEALTHY CONTROL CHILDREN. **A:** SHOWING PERCENT MEAN BIOFEEDBACK IMPROVEMENTS FOR PATIENTS IN ALL CONDITIONS COMPARED WITH BASELINE. ** WITHIN-GOUP DIFFERENCES (P<0.01; *** WITHIN-GROUP DIFFERENCES (P=0.001). **B:** SHOWING PERCENT MEAN BIOFEEDBACK IMPROVEMENTS FOR HEALTHY CONTROL CHILDREN IN ALL CONDITIONS COMPARED WITH BASELINE. ** WITHIN-GROUP DIFFERENCES (P<0.01); *** WITHIN-GROUP DIFFERENCES (P=0.001).

comparison baseline and therapist ($F = 66.442$; $p < 0.001$) and also for therapist and VR ($F = 16.26$; $p = 0.001$), but no statistical significant difference between VR and VR + THER ($F = 0.682$; $p = 0.422$). To break down the interaction, contrasts were performed comparing each condition across patients and healthy controls. These revealed significant interactions when comparing patients and healthy control values to baseline compared with THER ($F = 6.571$; $p = 0.022$) and to VR and VR + THER ($F = 5.025$; $p = 0.041$) but no significant effect to THER compared with VR ($F = 0.663$; $p = 0.428$).

Figure 14A and 14B show the mean motor output (measured as biofeedback values) improvement under all conditions compared with baseline for patients and healthy control subjects, respectively. Paired t-tests were analyzed separately for patients and healthy control subjects due to the main interaction effect (CONDITION x GROUP) of the ANOVA and were corrected for multiple comparisons ($N = 6$) as described in the methods section. For patients the biofeedback values revealed significant differences under all conditions compared with the total baseline condition (for THER $t = -3.852$, $p = 0.005$; for VR $t = -3.496$, $p = 0.008$ and for VR + THER $t = -5.051$, $p = 0.001$). Furthermore, significant results showed the comparison between VR and VR + THER ($t = -3.548$, $p = 0.009$), but not for both the comparison between therapist's instruction and VR ($t = 1.688$, $p = 0.135$) and for the combination of VR + THER with therapist's instructions alone ($t = 1.245$, $p = 0.253$). Similar results were found for healthy controls: paired t-tests revealed significant results for all supportive conditions compared with the total baseline condition (for THER $t = -7.539$, $p < 0.001$; for VR $t = -4.634$, $p = 0.004$,

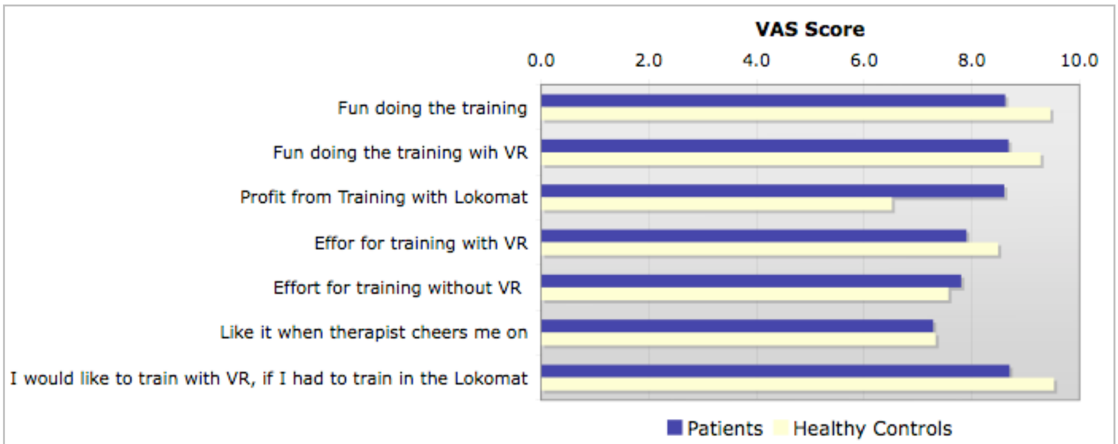

FIGURE 15: SUBJECTS OPINION ABOUT RAGT WITH VR. MOTIVATION TOWARDS RAGT WITH AND WITHOUT VR WAS EVALUATED FOR ALL SUBJECTS USING A SELF-DESIGNED WRITTEN QUESTIONNAIRE PRESENTED AS VAS.

and for VR + THER t = -3.799, p = 0.009). Furthermore, significant differences were revealed by comparison of THER and VR (t = 4.034, p = 0.007) but not for comparison of THER and the combination of VR + THER (t = 2.552, p = 0.043).

The analysis of the questionnaire (Figure 15) showed that all subjects had fun during the whole training session (mean for patients 8.7 points and for healthy control children 9.2 points, respectively). Healthy control subjects achieved slightly higher scores most of the time on the VAS than patients except for one question concerning profit from the Lokomat training. This may be because this question is aimed at RAGT with patients. It is difficult for healthy children to visualize the benefit of rehabilitation training. Patients and healthy control children reported somewhat less inspiration by therapists than during VR.

6.2.5 Discussion

The aim of this study was to compare the effect of different supportive strategies during robotic assisted gait training (RAGT) on the degree of active participation in children. This work investigated differences in therapy conditions on a single day and showed active participation during a short time period of two minutes. Within this period we showed that VR has the same immediate effect on motor output as therapist instructions in subjects with neurological gait disorders. Most importantly, the study revealed that both children with and without neurological disorders achieved significantly higher motor output during all supportive conditions as compared to walking without any motivational assistance. In other words, active participation was increased either by verbal encouragement given by a physical therapist (THER), by a VR soccer scenario or by the combination of both (VR + THER). It is not yet known whether such enhanced active performance can also be maintained over longer time periods or during a whole training session and whether this leads to a more effective rehabilitation process for patients. Furthermore, as there was no significant difference between the motor output measures and the three baseline measurements (walking without motivational assistance), it might be inferred that, with regard to the degree of active participation, the walking at the beginning of a therapeutic session is comparable to that at the end and shows no general fatigue effect. Although fatigue was not systematically verified fatigue during the training session, it might be interesting to include a fatigue score in further research.

It has been proposed that active training is more effective than passive training for motor learning and cortical reorganization[63]. Important findings in stroke patients suggest that simply moving or passively exercising the impaired limb does not lead to maximum recovery. Furthermore, it has become apparent that new motor skills, enriched, highly functional and task-oriented practice environments and primarily motivating tasks which increase engagement are necessary for motor re-learning and recovery after stroke[90]. Although children with CP might be substantially different in motor learning than those having experienced stroke or spinal cord injury, in cases in which the patients did have an intact and normally functioning nervous system prior to injury, it has been shown that activity, task-specificity and goal-orientedness are also crucial aspects in treatment of children with CP[99, 100].

Therefore, in RAGT it is essential that patients participate actively participation instead of just letting themselves "be walked". The patient's performance during the RAGT is difficult to estimate due to the loss of physical contact between therapist and patient[44, 96]. With the advanced biofeedback facility integrated in the Lokomat system used for the present study, we were able to record force interaction between the patient and the Lokomat and, on the basis of this data, to estimate the subject's performance. Although Lünenburger et al.[44] could demonstrate that biofeedback values are useful for evaluating and assessing the walking performance of subjects during Lokomat training, only the values for swing-phase correlated highly with the instructed activity, whereas the correlation of the stance-phase was less and sometimes even inversely correlated. Therefore, we recorded the four biofeedback values (bilateral hip and knee joints) during all conditions for the swing-phase only.

As outlined in the introduction, patient motivation plays a crucial role in determining therapy outcome, especially in the field of pediatric rehabilitation. The RAGT sessions, which consist of standardized monotonous walking for 30-45 minutes, are usually rather boring for children and can even be inconvenient. Hence, pediatric rehabilitation centers using RAGT try to boost patient motivation by showing DVDs or playing music. Such strategies, however, may distract children from the actual therapy, causing them to become completely passive in the Lokomat. VR techniques make it the possible to directly interlink the patients' motor performance during the gait training with actions in a computer-game-like virtual world. VR games adequately adapted to children's needs provide motivation and yet keep the focus on the actual gait training. Furthermore, the VR soccer scenario used is adaptable to children's individual skill levels and adjusts interactive elements to maximize motivation. In the current VR soccer implementation, the therapist could manipulate the opponent's speed offset and walking speed according to the skills of the participants. Assuming that a constant competitive situation could serve as a motivational factor, we included two different opponents in the present VR, one represents the first line of defense, over which the participant must kick the ball. The second approaches from behind and is able to take over the soccer ball from the avatar when he is in front.

In this study, we investigated the effect of adopting a VR scenario during RAGT based on the individual's level of active participation and compared this to a regular training session involving therapist encouragement and motivation. It should be pointed out, however, that the social interaction between a therapist and participant undoubtedly plays a crucial role, especially for patients. Thus the use of VR during rehabilitation therapy should not replace the physical therapist, but rather provide an additional means of enhancing training efficiency.

Children with neurological disorders as well as healthy controls achieved higher active participation levels not only with therapist encouragement but also with a VR soccer scenario during RAGT. Based on our clinical experience, the measurements gathered indicate that higher motivation and focused attention during RAGT have a positive influence on children's motor output, which in turn might lead to enhanced motor learning. Further research is required in this area.

Given that the four supportive conditions varied in patients and healthy control children, we will compare and discuss these conditions for the two groups separately.

Besides the fact that the mean motor output for patients revealed significant differences under all conditions involving motivational assistance compared with the normal walking condition, we also found significant differences between VR and VR combined with therapist instruction. All other comparisons of the supportive conditions exposed no significant differences.

It should be noted that the therapist's behavior during the two minutes of the "therapist-only" condition of the present study is not likely to be representative of normal behavior during a standard RAGT session of 30-45 minutes. In fact, motivating children during an entire training session is a very difficult and exhausting task and requires a great amount of engagement, creativity or even imagination. The use of a VR environment in RAGT, on the other hand, has the potential to constantly enhance and adapt training motivation and therefore increase active participation and training outcome. Moreover, VR may also be viewed as an additional medium used by the therapist to convey motivation and encouragement, e.g. by cheering when the patients' performance was particularly good or by encouraging the patient when something special must be achieved in the VR environment. This idea is in accordance with the fact that the combined condition VR+THER was significantly better than VR alone.

While mean active participation during baseline condition was similar for both groups, healthy control children achieved higher mean biofeedback values than patients for the condition therapist and the condition VR, but the difference was not significant. Furthermore, in healthy control children, there were significant differences between comparison therapist's instruction and VR values.

One explanation for the difference between patients and healthy children may be found in the safety system of the Lokomat. The device has built-in force monitoring which stops the robotic drives if the participants provide too much force input. These technical limitations influenced the measurements, primarily those of the healthy children because healthy children have more power than patients and therefore occasionally activated the safety mechanism. Hence, some conditions may be slightly underestimated in terms of motor output values. On several occasions, the force exerted under VR and VR plus therapist's instruction conditions triggered the Lokomat's safety mechanism. This led to frustration, which in turn caused the healthy children to reduce their force and therefore produce lower motor output values than would otherwise have been possible during the affected conditions. This may explain decreased results during VR and VR+THER conditions in healthy control subjects.

In order to gain knowledge about the patient's perspective regarding the motivational properties of the soccer scenario used during RAGT, participants were asked to complete a self-designed motivation questionnaire. Overall the answers submitted indicated that all participants had fun during RAGT, were highly motivated and had done their best.

We are aware of potential shortcomings in our study, one of which might be the choice of the tested schedule order. Although, attempts were made to alter the order of the conditions, the VR alone condition was always placed in the middle of the session. As a result, subjects always had some practice with the Lokomat system before participating in the VR condition, which might have improved their performance. Secondly, the patient group may be biased due to previous experiences with training on the Lokomat and also with VR scenarios. However, the positive results obtained with the VR soccer condition seem to indicate the motivational aspect of VR games. Other limitations of this study are the small sample size of the groups as well as the heterogeneous abilities of the patients. Therefore, it may be difficult to make generalizations regarding the benefit of using VR as a motivational tool in RAGT with other patient populations.

VR in rehabilitation has become a promising and useful adjunct to traditional therapy by providing objective quantification of the training process as well as safe environments which motivate children to exercise[68, 101]. The VR scenario presented has the potential to achieve higher motor outputs in children with neurological disorders as well as in healthy controls. Our observations support the idea that VR might be a promising supplement for RAGT in pediatric rehabilitation. However, further research and development is necessary in order to optimize such VR systems as a motivational tool and to investigate their clinical effectiveness in the rehabilitation process. Follow-up studies are needed in order to determine if the increase in active participation caused by patient cooperative strategies like VR leads to better clinical outcome. In addition, emphasis should be placed on the development of engaging and immersive game designs, which allow for human gait variability and performance levels. These variables must be optimized in order to keep children attentive during consecutive training sessions of 30-40 minutes.

In summary, the VR scenario used here has an immediate effect on motor output (biofeedback values) similar to one resulting from verbal instructions by a therapist. Therefore, VR represents a valuable tool to keep patients and healthy control children participating actively high during RAGT.

COMPETING INTERESTS

LZ and LL were employed by Hocoma AG, Volketswil, Switzerland, the producer of the Paediatric Lokomat. AMH has been reimbursed by the Hocoma AG, for attending two conferences as an invited speaker and received a fee for speaking at one conference.

AUTHORS' CONTRIBUTIONS

KB was involved in developing the study design, acquiring data, completing data analysis and drafting the manuscript. TS developed the study design, recruited subjects and performed data acquisition. AK, LZ, LL and RR developed the software and edited the manuscript. SK, AMH and LJ assisted with data interpretation as well as in revising the manuscript. All authors read and approved the final manuscript

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6.3 Publication: Study 2

Virtual Reality for Enhancement of Robot-Assisted Gait Training in Children with Neurological Gait Disorders

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6.3.1 Abstract

Objective: Examine the effect of various forms of training interventions, with and without virtual reality, on the initiation and maintenance of active participation during robot-assisted gait training.

Design: Intervention study at the Rehabilitation Centre Affoltern a. A., University Children's Hospital.

Subjects/Patients: Ten patients (5 males, mean age 12.47 years, SD 1.84 years) with different neurological gait disorders and 14 healthy children (7 males, mean age 11.76 years, SD 2.75 years).

Methods: All participants walked in the driven gait orthosis Lokomat® in four different randomly-assigned conditions. Biofeedback values calculated during swing phases were the primary outcome measure and secondary outcomes were derived from a questionnaire assessing the participant's motivation.

Results: Findings revealed a significant main effect for training condition in all participants ($p < 0.001$), for patients ($p < 0.05$) and for healthy controls ($p < 0.01$). Overall, both virtual reality-assisted therapy approaches were equally the most effective in initiating the desired active participation in all children compared to conventional training conditions. Motivation was very high and did only differ between the groups in the virtual navigation condition.

Conclusion: Novel virtual reality-based training conditions represent a valuable approach to enhance active participation during robot-assisted gait training in patients and healthy controls.

Key words: virtual reality, rehabilitation, robot-assisted gait training, motivation, children, neurological gait disorders

6.3.2 Introduction

Over the past decade, robotic devices have become increasingly established for gait training in patients with neurological gait disorders. Several studies demonstrated improvements in locomotor ability in different patient populations receiving robot-assisted gait training (RAGT)[50-53, 55, 56]. Nevertheless, the literature so far appears to be controversial. Recently published randomized controlled trials showed the effectiveness of RAGT and promising effects on functional and motor outcomes in patients after stroke[51, 57]. In contrast, a multicenter randomized clinical trial found that conventional gait training appeared to be more effective for stroke patients than RAGT[58]. There is also a growing body of literature showing that RAGT for children with cerebral palsy is feasible and can be considered a save treatment method with beneficial effects on the standing and walking sections of the gross motor function measurement (GMFM)[59, 60]. Explanations for the controversial results might be on the one hand due to different patient populations and on the other hand due to different methods for enhancing activity during training interventions and protocols (e.g. reducing body-weight support, increasing gait speed, reducing guidance force). Overall, training efficacy depends on a number of different parameters. Findings of RAGT need to be interpreted cautiously and examined in greater detail to fully exploit its beneficial effect in each specific patient population.

Another possible explanation for the limited effectiveness of robotic devices might be the patient's passivity in the driven gait orthosis (DGO). Studies have shown that active involvement in the production of a motor pattern resulted in greater motor learning and retention than passive movement[62-64]. Comparison of RAGT with manually assisted treadmill training has shown that muscular activity in patients and healthy controls were reduced when walking with a robotic device [102, 103]. An important issue in RAGT might be preventing passivity and improving active performance in the rehabilitation training of patients. A prerequisite for achieving these targets is the appropriate feedback of patient performance. Virtual reality (VR) offers a novel possibility to provide feedback to patients about their performance and the opportunity to directly interlink the patient's motor performance during RAGT with actions in a computer game-like virtual world. Especially in pediatric rehabilitation the need of diversification, fun and motivation have been demonstrated in several investigations[93, 94]. Previous studies indicated that VR offers powerful options to provide therapy within a functional, purposeful and motivating context[2, 66, 95]. The effectiveness of RAGT in children might be strongly influenced by their motivational state during the intervention. Motivation is an interaction between a person's motives and the incentives of a situation[104]. As changing a person's motive is difficult, a solution could be to influence and provide incentives during RAGT.

Given that the motivational state is a precondition for the success of such an approach, we sought to ascertain whether VR-based therapy in patients more easily induces an appropriate response during RAGT as compared to conventional training interventions without VR. The purpose of this study was to examine the differential effect of various VR scenarios as well as verbal encouragement on the induction and maintenance of active participation during RAGT. We assume that competitive situations and augmented feedback could serve as additional motivational factors and therefore will lead to higher active participation and maintenance during conditions with VR compared to other conventional interventions without VR in pediatric rehabilitation.

6.3.3 Methods

6.3.3.1 Participants

The study was approved by the local Ethics committee and conformed to standards set by the Declaration of Helsinki. Written informed consent was obtained from the legal guardians of all participants before inclusion in the study. A total of 24 participants met the inclusion criteria and were enrolled in the study. Ten patients (five males, mean age 12.2 years, SD 2.04 years) with various neurological gait disorders were referred to the *Rehabilitation Centre Affoltern am Albis* of the University Children's Hospital Zurich. Additionally, 14 healthy children (seven males, mean age 11.78 years, SD 2.72 years) from the soccer club *Affoltern am Albis*, Switzerland, were included. The demographic characterization of the participants is given in Table 5.

All participants were naive to the purpose of the study and were eligible for the study when meeting the following inclusion criteria: (1) aged 4-18 with a femur length between 21 and 47cm (2) minimal voluntary control (i.e. the ability to initiate voluntarily a step movement) of their lower-extremity muscles to ensure that they had the ability to respond and adapt their walking pattern and could follow different walking instructions (3) ability to signal pain, fear, discomfort and (4) willingness to meet the study requirements for training with the DGO Lokomat® (Hocoma AG, Volketswil, Switzerland).

TABLE 5: CHARACTERISTICS OF PARTICIPANTS

ID	**Age (yr)**	**Sex**	**Height (cm)**	**Weight (kg)**	**Lokomat®'s Legs** K = kids T = Teens	**Disease**	**GMFCS-Level**	**Over ground mobility aids**
01	13	f	149	41,4	T	BS-CP	II	none
02	13	m	154	53,0	T	TBI	-	AFOs
03	16	f	164	56,4	T	SLE	-	none
04	9	m	133	21,7	K	BS-CP	III	AFOs
05	11	f	142	38,0	T	BS-CP	III	AFOs
06	13	f	153	58,0	T	MMC	-	KAFOs
07	12	f	160	48,0	T	MMC	-	KAFOs, post walker
08	11	m	152	40,0	T	TBI	-	Wheelchair
09	10	m	140	37,0	K	BS-CP	IV	Wheelchair, AFO
10	14	m	144	29,0	K	BS-CP	II	Insoles
11	15	f	169	58,5	T	healthy	-	none
12	14	f	169	49,0	T	healthy	-	none
13	14	f	166	60,0	T	healthy	-	none
14	11	m	135	34,0	K	healthy	-	none
15	11	m	140	31,0	K	healthy	-	none
16	6	f	125	28,0	K	healthy	-	none
17	15	f	174	65,0	T	healthy	-	none
18	10	m	146	37,0	K	healthy	-	none
19	10	m	148	39,8	K	healthy	-	none
20	10	m	144	33,7	K	healthy	-	none
21	10	m	139	30,5	K	healthy	-	none
22	10	m	146	34,2	K	healthy	-	none
23	15	f	158	50,4	T	healthy	-	none
24	14	f	164	57,6	T	healthy	-	none

Abbreviations: GMFCS-Level = Gross Motor Function Classification System; BS-CP = Bilateral Spastic Cerebral Palsy; MMC = Meningomyelocele; TBI = Traumatic Brain Injury; SLE = Systemic Lupus Erythematodes; AFOs= Ankle-Foot Orthosis; KAFOs = Knee-Ankle Foot Orthosis

6.3.3.2 Interventions

All measurements were conducted at the Rehabilitation Centre Affoltern a. A. of the University Children's Hospital Zurich, Switzerland. Prior to the measurements, the participants became familiarized with the Lokomat. For clinical use, the Lokomat is normally position-controlled with 100% guidance force. The intervention protocol was held constant and each child was unloaded with 30% of their individual body-weight with 100% guidance force and foot-lifting straps, which assisted ankle dorsiflexion for adequate toe-clearance during the swing phase. Participants had a velocity of 1.8km/h, except for one patient (ID 07) who had a reduced speed of 1.6km/h.

Then, all participants were randomly-assigned to one of the two test schedules. Measurements consisted of two parts. First, participants were instructed to walk in three different activity levels for 30 seconds each to ascertain the individual degree of active involvement (Validation): (a) passive: Participants should behave completely passively. (b) active: participants should walk with the same pattern as the Lokomat (c) strong active: participants should exaggerate their walking with maximal force. All instructions for the validation were standardized. The second part consisted of four pseudo-randomly presented conditions: (1) use of a VR soccer game as a motivating tool to walk actively (VR soccer) (2) with therapist's standardized instructions to promote active walking (Therapist) (3) watching a movie (DVD), and (4) use of the VR navigation game as a motivating tool to walk actively (VR navigation) (Figure 16). Instructions for the second part were kept as standardized as possible during all seven-minute conditions.

FIGURE 16: MEASUREMENT SCHEDULES OF THE TWO PARTS. PARTICIPANTS WERE RANDOMLY ASSIGNED TO EITHER OF THE TWO SCHEDULES.

6.3.3.3 Virtual Environment System Setup

Both VR scenarios have been developed to increase motivational aspects especially for RAGT in paediatric rehabilitation. The VR setup consisted of a 42-inch flat screen placed in front of the Lokomat and a 7.1 Dolby surround system. The Lokomat system was used as a multimodal feedback system: The man-machine interaction forces measured from the Lokomat are used as an input device of the patient's movements into the VR. Furthermore, the Lokomat served as a haptic display that reflects interactions with objects, such as a soccer ball, represented in the virtual environment with the purpose of providing haptic feedback to the participant. The haptic contact forces when kicking the ball were modeled as a spring damper system.

The VR soccer game made it possible for participants to kick a ball in competition against two virtual opponents (Figure 17A). One was waiting in front of the participant, who had to kick the ball past his opponent, otherwise he had to start from the last kick position. The second would approach from behind, taking over the soccer ball when he outpaced him. This second opponent was configured to walk faster and take over the ball from the participant if the exertion of the participant was weak. The opponent walked slower when the child participated actively.

The VR navigation game used asymmetric physical activity of the legs to induce turning in the virtual environment (Figure 17B). To be specific, turning right and left can be induced by increasing activity of the contralateral leg of the desired direction, and decreasing activity of the ipsilateral leg, respectively.

FIGURE 17: BOTH VR GAMES USED IN THIS STUDY. (A) VR SOCCER GAME WITH TWO OPPONENTS (B) VR NAVIGATION GAME.

6.3.3.4 Outcome Measures

The Biofeedback of the Lokomat gait orthosis is based on the interaction torques between the participant and the orthosis. For this reason, the hip and knee linear drives are equipped with force sensors that measure man-machine interaction forces that are required to keep the participant on a predefined gait trajectory. The biofeedback values are unit less and weighted averages of the measured man-machine interaction forces at the hip and knee joints for stance and swing phase. The weighting functions were defined for each part of the gait cycle, such that the resulting biofeedback values increase for therapeutically desirable movements, e.g. knee flexion for early swing. Thus, the biofeedback levels are positive when the patient is actively participating and negative for passive behavior or when inappropriate involuntary muscle activations such as caused by spasms would interfere with the gait cycle. Although these latter can not be differentiated by the driven gait orthosis, strong timely inadequate forces would trigger the Lokomat's safety stop mechanism. For the present study, we assumed that the force level represents the physical activity of the participants[44, 80].

We recorded eight biofeedback values (bilateral hip and knee joints) separately for swing- and stance-phases during all conditions. The mean biofeedback value of the swing- and stance phase for hip and knee joints was calculated separately during each condition. This provided four overall biofeedback values for hip and knee joints and for swing- and stance phases in each condition (i.e. VR soccer, VR navigation, Therapist, DVD) separately.

To assess subjective aspects of the RAGT with and without VR a self-designed motivational questionnaire was used. Patients and healthy controls were asked to rate on a visual analogue scale (VAS) the extent to which they had liked the different training conditions from 0 ("not at all") to 10 ("very much").

6.3.3.5 Statistical Analysis

The individual "involvement" was analyzed using Spearman's correlation because non-linear relations had to be expected. Biofeedback values for all four joints in the two gait phases swing and stance during about 580 strides for each subject were correlated to the level of activity that each subject was instructed to perform (1 = passive, 2 = active, 3 = strong active). Other settings (body weight support, treadmill speed, patient coefficient) that might have influence on the biofeedback values were kept constant.

Biofeedback values were examined for normality. As the assumption for normally distributed data was not met, nonparametric Friedman-Test was performed to detect differences among the conditions, while post-hoc analysis was performed using Wilcoxon signed rank for comparisons between the conditions[105]. In general, effects were considered statistically significant when falling below $p < 0.05$. Since p-values strongly depend on sample sizes we additionally calculated the effect size measure Cohen's d to obtain information on how strong an effect is[105, 106]. In this study we decided to rely on strong effect sizes for our interpretation. In terms of Cohen’s terminology $d \geq 0.5$ can be considered as medium effect, while $d \geq 0.8$ can be considered as large effect.

With respect to the questionnaire, averaged values (±SD) for the motivation scores were calculated and differences between the conditions (within each group) were analyzed with Friedman’s test. Pair-wise comparisons between the conditions were additionally analyzed with the Wilcoxon signed rank test. Furthermore, motivational scores for each individual condition were compared between the two groups and analyzed with the

Mann-Whitney U-test. All statistical analyses were performed using the statistical software package SPSS 16 for Mac, release 16.0.1.

6.3.4 Results

The two groups assessed in this study did not differ significantly in age (p=0.689), gender (p=0.735), height (p=0.812), and weight (p=0.852) from each other in the demographic characteristics given in Table 5.

The recorded biofeedback values were correlated to the level of activity each subject was instructed to perform ("passive" = 1, "active" = 2, "strong active" = 3). Figure 18 shows absolute biofeedback values of hip swing for the instructed activity using clustered bars. Biofeedback activity for the passive condition (mean ± SD) was 11.20 ± 18.91 (patients) and 4.17 ± 7.52 (healthy children), respectively. During active condition the values were 20.60 ± 10.32 (patients) and 34.71 ± 16.65 (healthy children). For the strong active condition the values were 54.96 ± 20.22 (patients) and 65.36 ± 25.27 (healthy children).

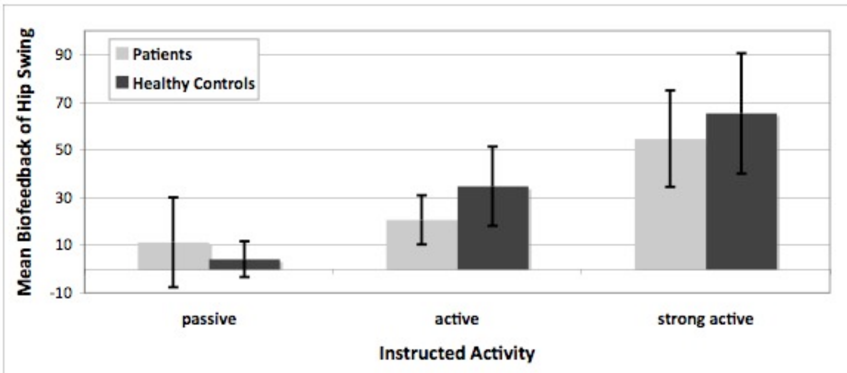

FIGURE 18: DIFFERENCES BETWEEN THE MEAN BIOFEEDBACK VALUES OF HIP SWING PHASE BROKEN DOWN FOR INSTRUCTED ACTIVITY SEPARATELY FOR PATIENTS AND HEALTHY CONTROL CHILDREN.

The biofeedback values of the hip torques correlated moderately with the instructed activity during swing phases, whereas there was no correlation of hip and knee torques and activity during stance phases. Results are illustrated in Table 6. Based on the results from the correlation between instructed activity and biofeedback values (Table 6), further analyses were done for the biofeedback values during the hip swing phase only.

TABLE 6: CORRELATION OF BIOFEEDBACK AND PARTICIPANT'S INSTRUCTED ACTIVITY

Joint	Hip right		Knee right		Hip left		Knee left	
	Stance	Swing	Stance	Swing	Stance	Swing	Stance	Swing
Spearman 's rho	0.135	0.560	0.145	0.217	0.200	0.654	0.098	0.142
Sig. (2-tailed)	0.258	0.001*	0.225	0.067	0.093	0.001*	0.412	0.233

*p<0.001

Significant differences in biofeedback values were found both for the patient group and for the healthy controls (see Table 7).

TABEL 7: ANALYSIS OF THE BIOFEEDBACK VALUES OF THE HIP SWING PHASE

Group	Biofeedback values of the hip swing phase VR Soccer Mean (SD)	 VR Navigation Mean (SD)	 Therapist Mean (SD)	 DVD Mean (SD)	Within group differences
Patients	18.96 (15.97)	24.90 (21.97)	10.52 (12.80)	6.12 (13.79)	χ^2= 8.76 p = 0.033**
Healthy Controls	43.73 (24.51)	31.51 (22.49)	30.63 (24.80)	23.03 (22.39)	χ^2= 15.00 p = 0.002
Between group differences	z = -2.635 p = 0.008**	z = -1.23 p = 0.219	z = -2.459 p = 0.014*	z = -1.932 p = 0.053	

*p<0.05; **p<001. SD: standard deviation; VR virtual reality.

In addition, Table 7 shows the differences of the absolute biofeedback values during the four conditions. Patients reached the highest biofeedback values (mean, SD) in the two VR conditions and the lowest values for the DVD condition, whereas healthy children reached the maximum biofeedback value for the condition VR soccer and the lowest values for the DVD condition.

A post-hoc analysis was performed to determine differences between the conditions (Figure 19). Statistical comparisons of both VR conditions with DVD revealed significant results in both groups (for VR soccer: p<0.001, p<0.05 for patients respectively; VR navigation: p<0.05). Comparisons of VR conditions with therapist showed only a significant difference in the healthy control group for VR soccer (p<0.05).

Similarly, for the comparisons of therapist conditions compared with DVD: only healthy controls ($p<0.05$) showed significantly more active performance in the therapist condition.

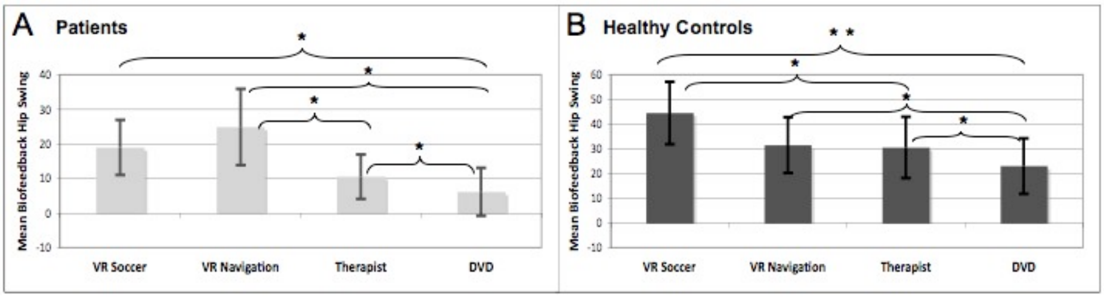

FIGURE 19: COMPARISON (MEAN ± SD) OF HIP SWING PHASE IN ALL FOUR CONDITIONS SEPARATELY FOR (A) PATIENTS (1-TAILED) AND (B) HEALTHY CONTROL CHILDREN. ASTERISKS ABOVE THE COLUMNS DEFINE THE LEVEL OF SIGNIFICANCE OF WITHIN-GROUP COMPARISONS (** P<0.001; * P<0.05).

Effect sizes for patients for the comparison of both VR conditions with DVD (for VR soccer: Cohen's d = 0.86 and VR navigation: d = 1.03) were considered as large and VR with therapist (VR soccer: d = 0.58 and VR navigation: d = 0.80) were considered as medium and large, respectively. Only the effect size for the comparison of therapist with DVD (d = 0.33) must be considered small. A similar pattern appeared for healthy children: the effect size for VR soccer compared with DVD (d = 0.88) was large. Effect sizes for all other within-group comparisons were considered medium, beside the comparison of therapist with DVD (d = 0.32) was considered small.

The analysis of this motivation questionnaire revealed that during each condition, all participants had fun. The Friedman's test showed only a significant difference between the conditions for the healthy control group. Pair-wise comparisons showed that the healthy children rated the VR soccer (p=0.012) and watching a DVD (p=0.042) significantly higher than the instructions by the therapist. We found only one significant difference between the groups for the VR navigation condition (Table 8). With regard to generalization of the preferred conditions 70.4% of all participants reported that they would prefer the VR for the next training sessions, while only 29.6% preferred watching a DVD.

TABLE 8: ANALYSIS OF THE MOTIVATION QUESTIONNAIRE

Group	Motivation scores VR Soccer Mean (SD)	VR Navigation Mean (SD)	Therapist Mean (SD)	DVD Mean (SD)	Within group differences
Patients	8.78 (1.59)	6.97 (3.12)	7.80 (3.06)	9.25 (2.37)	$\chi^2 = 5.548$ p = 0.136
Healthy Controls	9.71 (0.47)	9.36 (0.89)	7.71 (3.45)	9.54 (0.80)	$\chi^2 = 9.434$ p = 0.024*
Between group differences	z = -1.568 p = 0.117	z = -2.020 p = 0.043*	z = -0.030 p = 0.976	z = -0.907 p = 0.364	

*p<0.05. SD: standard deviation; VR: virtual reality.

6.3.5 Discussion

Active participation is an important prerequisite for motor learning and improving functional and motor outcomes. To assess participation during RAGT and to find the most effective and most strongly motivational interventions in paediatric rehabilitation is of interest to both therapists and clinicians. In the present study, VR-based training was implemented for RAGT in children. The overall aim of the present study was to investigate the effect of different supportive conditions on active participation and maintenance in children during RAGT. The two VR-assisted therapy forms resulted equally in the desired response in both patients and healthy controls. The between-group analyses showed that the effects were equal between healthy subjects and patients. Furthermore, in this study we were able to extend recent observations[107] that VR-based RAGT has an advantage over other conventional training sessions, especially in longer lasting conditions of seven minutes.

Biofeedback of the hip swing phase correlated moderately with the instructed activity in all participants. There was no correlation for the knee swing phase and for the hip an knee stance phases. Despite the fact that variables were kept constant, the relative low correlations might have been partially caused by difficulties in the exact synchronization of the exoskeleton and the treadmill and the contact of the foot with the treadmill during stance phase. These findings are in line with those from Lünenburger et al. and Banz et al.[44, 80, 81]. For these reasons further calculations were based only on hip swing phases.

The results reported here support our earlier findings that RAGT coupled with VR can improve active participation in children[107]. We extended these findings by demonstrating that VR during RAGT was able to maintain the enhanced active participation level also during prolonged training conditions of seven minutes. In particular, both VR conditions (soccer game and navigation game) reached higher participation levels compared to normally applied training conditions, such as therapist instructions or watching a DVD in both patients and healthy children. The lowest biofeedback values were revealed in the condition DVD, although children reported that they liked watching a DVD very much (as reported in the motivation questionnaire). The reason for this discrepancy may be that children fully immersed themselves in watching a DVD but were not concentrated on their walking behavior and "let themselves go" by the Lokomat instead of performing actively. This might be one of the main advantages of VR coupling with RAGT. The question arises as to the possible aspects/mechanisms involved in imparting the beneficial effects of VR supported RAGT to children.

Although motivation has long been suspected to play an important role in determining the outcome of therapy, a clear definition of this phenomenon has not yet been drawn up[78]. Motivation is usually not a constant factor but a dynamic process that is dependent on many external and internal factors. Awareness of all the factors impinging on motivation for rehabilitation will also foster a better understanding of the phenomenon of patient disengagement in rehabilitation[78]. In particular, active engagement towards a training intervention is usually equated with motivation, and similarly passivity with the lack of motivation[108]. Several studies could demonstrate that virtual environments are challenging to children and help them to be creative which proved to be motivating[93, 107] and helped patients with cerebral palsy to develop a more positive self-image[67, 94, 109]. A recently published review concluded that due to the engaging and challenging character of VR, it seems to be an effective rehabilitation tool in pediatric rehabilitation, as it allows children to participate in activities, which would otherwise not be possible[70].

Although little is known about the neural mechanisms of locomotor recovery, VR might target brain networks speeding up the recovery process[92, 110]. Indeed, using functional magnetic resonance imaging, You et al.[23] demonstrated that VR induced cortical reorganization in the lower extremity of patients with chronic stroke. These findings suggest that VR may have attributed to positive changes in neural reorganization.

In our previous study[107], we were able to show that a VR-based soccer scenario induced an immediate effect on motor output that was of similar magnitude as the effect resulting from verbal instructions by the therapist. However, one has to be aware that each given condition in this study lasted for about two minutes. While an average normal training period lasts about 30 – 40 minutes, a two-minute experimental condition is not likely to be representative. Therefore, we extended the duration of the conditions up to seven minutes, which was the longest possible duration to compare several conditions within a single therapy session.

While the current study provides findings about improvements in active participation of VR-based RAGT in children, this study clearly has potential shortcomings. First, as previously mentioned, each condition lasted 7 minutes, while patients walk up to 45 minutes during a normal RAGT session. To the best of our knowledge, it has not yet been shown whether this enhanced active performance can also appear during a whole training session and whether this leads to a more effective rehabilitation process for patients. Secondly, patients were heterogeneous in respect to age and diagnosis. However, this reflects a normal pediatric neurorehabilitation clinic population and the healthy control group was matched for age and gender. Thirdly, unfortunately, the two game scenarios provided suspense for only 15 minutes, after which the children lost interest in the game. Indeed, emphasis should be placed on the development of engaging and immersive game designs, which allow and even promote human gait variability and various degrees of difficulty in performance levels. These variables must be optimized in order to keep children attentive during consecutive training session of 30-40 minutes. Furthermore, cognitive and spatial aspects could be implemented in serious games designs to increase the therapeutic value of such VR games.

In conclusion, VR-based scenarios were implemented for RAGT in children. The results have demonstrated that patients with neurological gait disorders and healthy controls participated more actively with VR-based RAGT than with other interventions. The VR scenarios of this study were designed to challenge children's abilities and provided interactive elements to engage them during Lokomat therapy. Further research should reveal whether an increase in active participation leads to a better functional outcome, as a result of patient cooperative strategies such as VR. However, to enable this kind of research, visionary and thoughtful game designs first need to be developed.

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6.4 Publication: Study 3

Influencing Stance Phase Activity in Children During a Virtual Reality Based Robot-Assisted Gait Training

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submitted

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6.4.1 Abstract

Objective: During rehabilitation, it is often difficult to train balance and weight bearing during single leg stance in children with neurological gait disorders, especially in dynamic conditions. The objective was to determine changes in stance phase activity of the supporting leg performing a soccer kick during a virtual reality-based robot assisted gait training (RAGT).

Design: Case-control study with a single RAGT intervention.

Setting: Rehabilitation Center for Children and Adolescents in Affoltern am Albis, Switzerland.

Participants: Ten patients (mean age 12.57 ± 1.92 years) with neurological gait disorders and 13 age-matched healthy children (mean age 11.47 ± 2.64 years).

Intervention: Comparisons of participant's kicking activity during RAGT were made between (i) the patients and the healthy children, and (ii) between children who could induce large leg activations during regular steps and those who could not.

Main Outcome Measures: Biofeedback (BF) values calculated from force sensors at hip and knee drives at the Lokomat® quantifying man-machine interaction forces for stance and swing phase.

Results: During RAGT, the supporting leg of healthy children showed smaller BF values during kick steps compared to normal steps ($p < 0.001$), whereas patients showed no differences ($p = 0.85$). Children who could induce large leg activations revealed significant smaller BF values during kick steps ($p = 0.004$).

Conclusions: The smaller BF values during kick steps compared with normal steps indicated that especially participants with relative good coordinative capacity stabilized their supporting leg, thereby concurrently enhancing training of the supporting leg. Unfortunately, this appeared difficult for most patients.

Keywords:

Virtual reality, robot assisted gait training, stance phase activity, children, motivation.

List of Abbreviations

RAGT	robot assisted gait training
BWSTT	body-weight supported treadmill training
VR	virtual reality
BF	biofeedback

6.4.2 Introduction

An impaired walking ability is frequently observed in patients with neurological gait disorders. Recent achievements in rehabilitation engineering resulted in the development of several robotic systems that aim to improve walking ability in these patients[111]. Nowadays, robot assisted gait training (RAGT) appears promising, as it enables patients to train more frequent and prolonged, while simultaneously relieving therapists from physical demands compared with manually assisted bodyweight supported treadmill training (BWSTT). However, current literature is controversial regarding the effectiveness of RAGT in adult patients. While some studies reported advantages of RAGT compared with manual BWSTT or conventional physical therapy[51, 52, 55, 57, 112], others found the opposite[58, 113]. It remains therefore unclear which locomotor training intervention might be more effective in restoring walking function in adult patients with neurological disorders[114].

In the field of pediatric neurorehabilitation, there is a growing body of literature suggesting that RAGT is a feasible and safe treatment option for children with cerebral palsy with potential beneficial effects on standing and walking[54, 59, 60]. In addition, one randomized trial showed positive effects of RAGT compared to conventional therapy[61]. Despite these promising results, clinical experiences showed that children, who performed the monotonous RAGT on a daily basis, rapidly lost their motivation to be actively engaged. To counteract this problem, virtual reality (VR) was applied offering a powerful option to provide therapy within a functional, purposeful and motivating context[2, 66, 107, 115-117]. Indeed, adding virtual environments to RAGT can enhance motivation of the patients[97, 107, 115] and it offers the possibility to individualize treatment needs while providing standardization of assessments and training protocols[66]. Furthermore, the use of VR provides an opportunity for the physically disabled patients to participate actively in challenging activities, which are under normal circumstances difficult to perform safely[67-69].

In the current study, we implemented a VR soccer game, which was specifically designed to playfully train both legs during gait training[115, 116]. In real life, kicking a ball can be quite a challenge to perform, as the kicking leg becomes trained in a dynamical way, while the weight bearing capacity and stability of the supporting leg becomes trained by the prolonged single stance duration[118, 119]. Under real life circumstances, such a movement is difficult to perform or even threatening for children with neurological gait disorders, as it could result in a fall. Within RAGT this is not an issue as the harness ensures safety.

The objective of this study was to determine changes in stance phase activity of the (more affected) supporting leg, while performing a soccer ball kick during VR-based RAGT in children with neurological gait disorders. Furthermore, we suggest that a prolongation of the stance phase during the kick would indicate that the young patients would more or less automatically train the weight bearing capacity of the supporting (more affected) leg, while they were concentrating on performing a kick with the less affected leg during the soccer game.

6.4.3 Methods

6.4.3.1 Participants

The study was approved by the cantonal Ethics committee and conformed to the Declaration of Helsinki. Written informed consent was obtained from the legal guardians of all participants before inclusion in the study. All measurements were conducted at the Rehabilitation Center for children and adolescents in Affoltern am Albis of the University Children's Hospital Zurich, Switzerland.

Patients with neurological gait disorders and referred to the Rehabilitation Center for RAGT were screened for eligibility (no contra-indications for performing RAGT and the cognitive capacity to understand instructions). Healthy age-matched children from a soccer club who are trained in kicking movements were contacted to attend the study. In total, 26 children (12 patients with neurological gait disorders and 14 healthy children) participated in this study. All performed a single training session with the rehabilitation robot Lokomat® (Hocoma AG, Volketswil, Switzerland) including seven minutes with the VR-based soccer scenario. Three participants dropped out due to recording failures (2 patients and 1 healthy child). Table 9 shows demographic characteristics of the 10 patients (6 boys, mean age 12.57 years, SD 1.92 years) with different neurological gait disorders and 13 healthy children (7 boys, mean age 11.47 years, SD 2.64 years).

TABLE 9: CHARACTERISTICS OF PARTICIPANTS

ID	Age (yr;m)	Sex	Height (cm)	Weight (kg)	Lokomat® Legs	Kick leg	Speed Km/h	Disease	GMFCS -Level	Over ground mobility aids
01	14;3	m	163	63.0	T	re	1.8	MMC	-	Crutches
02	13;3	f	153	58.0	T	re	1.8	MMC	-	KAFOs
03	11;7	f	160	48.0	T	re	1.6	MMC	-	KAFOs, walker
04	10;0	m	133	21.7	K	li	1.8	spastic diplegic CP	III	AFOs
05	11;4	f	142	38.0	T	re	1.8	spastic tetrapareses CP	III	AFOs
06	13;7	m	144	29.0	K	li	1.8	spastic tetrapareses CP	II	Insoles
07	10;4	m	140	37.0	K	li	1.8	spastic tetrapareses CP	IV	Wheelchair, AFOs
08	13;4	m	166	55.5	T	li	1.8	TBI	-	AFOs
09	11;4	m	152	40.0	T	re	1.8	TBI	-	Wheelchair
10	16;1	f	164	56.4	T	re	1.8	SLE	-	no
11	14;2	f	169	49.0	T	re	1.8	healthy		none
12	14;2	f	166	60.0	T	re	1.8	healthy		none
13	11;0	m	135	34.0	K	li	1.8	healthy		none
14	10;5	m	140	31.0	K	re	1.8	healthy		none
15	6;0	f	125	28.0	K	re	1.8	healthy		none
16	15;2	f	174	65.0	T	re	1.8	healthy		none
17	10;1	m	146	37.0	K	re	1.8	healthy		none
18	10;0	m	148	39.8	K	re	1.8	healthy		none
19	9;5	m	144	33.7	K	re	1.8	healthy		none
20	10;2	m	139	30.5	K	re	1.8	healthy		none
21	10;1	m	146	34.2	K	re	1.8	healthy		none
22	13;8	f	158	50.4	T	re	1.8	healthy		none
23	14;3	f	164	57.6	T	li	1.8	healthy		none

Abbreviations: K = Kids; T = Teens; GMFCS-Level = Gross Motor Function Classification System; CP = Cerebral Palsy; MMC = Meningomyelocele; TBI = Traumatic Brain Injury; SLE = Systemic Lupus Erythematodes; AFOs = Ankle Foot Orthosis; KAFOs = Knee-Ankle Foot Orthosis

6.4.3.2 The driven gait orthosis Lokomat®

The Lokomat® comprises of two actuated leg orthoses attached to the participants' legs. Each orthosis has linear drives in hip and knee joints to move the participants' leg in a physiological walking pattern. All participants wore passive foot lifters that provided sufficient ankle dorsiflexion during the swing phase and prevented stumbling. The Lokomat's® exoskeleton with "teens' legs" was used for adolescent participants (femur length: 0.35-0.47m), while children used pediatric "kids' legs" (femur length: 0.21-0.35m). A bodyweight support system allowed reducing the effective bodyweight by a definable amount. Throughout the study, participants walked with 30% of body-weight support, 100% constant guidance force by the Lokomat® and a velocity of 1.8 km/h, except for one patient who had a reduced speed of 1.6 km/h.

6.4.3.3 Virtual Environment System Setup

The VR setup included a 42inch flat screen and a 7.1 Dolby surround system. The graphic elements were programmed using the Ogre framework (www.ogre3d.org). The sound output was rendered using the Fmod programmers API (www.fmod.org) and the graphics models were created in Maya (www.adobe.com). The Lokomat® was used as a multimodal feedback system: The man-machine interaction forces measured from the Lokomat® were used as an input device of the patient's movements into the VR. Furthermore, the Lokomat® served as a haptic display that reflected interactions with objects, such as a soccer ball, represented in the virtual environment with the purpose of providing haptic feedback to the participant[84]. The VR soccer scenario provided the possibility to kick a soccer ball in competition against one or two virtual opponents (Figure 20). The VR game was set up individually, so that during seven minutes, every patient had to kick the virtual ball about 25 times with their preferred and less affected leg.

FIGURE 20: PATIENT IN THE LOKOMAT® WITH THE VIRTUAL REALITY SOCCER GAME.

6.4.3.4 Outcome Measure

The main outcome measure was the biofeedback (BF) of the Lokomat® gait orthosis. The BF values are based on the interaction torques between the participant and the orthosis. For this reason, the hip and knee linear drives are equipped with force sensors that measure man-machine interaction forces that are required to keep the participant on a predefined gait trajectory. The BF values are unit-less and weighted averages of the measured man-machine interaction forces at the hip and knee joints for stance and swing phase[45]. During the swing phase, high BF values indicated large and desired interaction forces (i.e. timely correct and supportive of the intended movement of the driven gait orthosis). Negative BF values occurred when forces were applied that counteracted with the intended movement of the robotic leg. Further details of the BF computation can be found in[44, 45, 81].

During stance phase, however, the situation is more complex due to the interaction between the foot and the treadmill. During a kick step, a prolonged stance phase is induced and the supporting leg takes over weight for a longer time (compared to a regular step in the Lokomat® system). This should result in smaller BF values, as prolonged stance duration would negatively infer with the walking pattern implemented in the Lokomat®. We hypothesized therefore that if subjects were able to train the weight bearing capacity of their supporting leg during a kick step, a prolonged stance step[119] and smaller BF values during stance should be found. To estimate the magnitude of the stance step, we calculated the position where the stance foot contacted the treadmill during initial contact using geometrical data (the upper and lower leg length and the joint angles of hip and knee at the time of the heel strike). A larger stance step occurred, when the foot position during initial contact was further in front on the treadmill.

6.4.3.5 Data Analysis

BF values for each hip and knee joint were recorded separately for the swing and stance phase of the supporting and kicking leg, both for normal steps as well as for steps where the participants kicked the virtual ball.

For each subject, the BF values for each gait phase, each leg and separated for steps (kick stride versus normal steps) were calculated over 25 steps. These resulted in 16 different BF values. As previous studies showed that the most reliable BF values were derived from the hip joint during the swing phase[44, 81], we used these values to divide the participants in two groups, (1) those who could correctly induce large leg activations ("high activity") indicative good motor control and strength and (2) those who could not ("low activity"). Grouping was performed according to a two-step cluster analysis using BF values of the hip swing phase during normal steps of both legs (see Figure 21). Grouping was therefore independent from the BF values derived during stance phase, which were the outcomes of interest for this study.

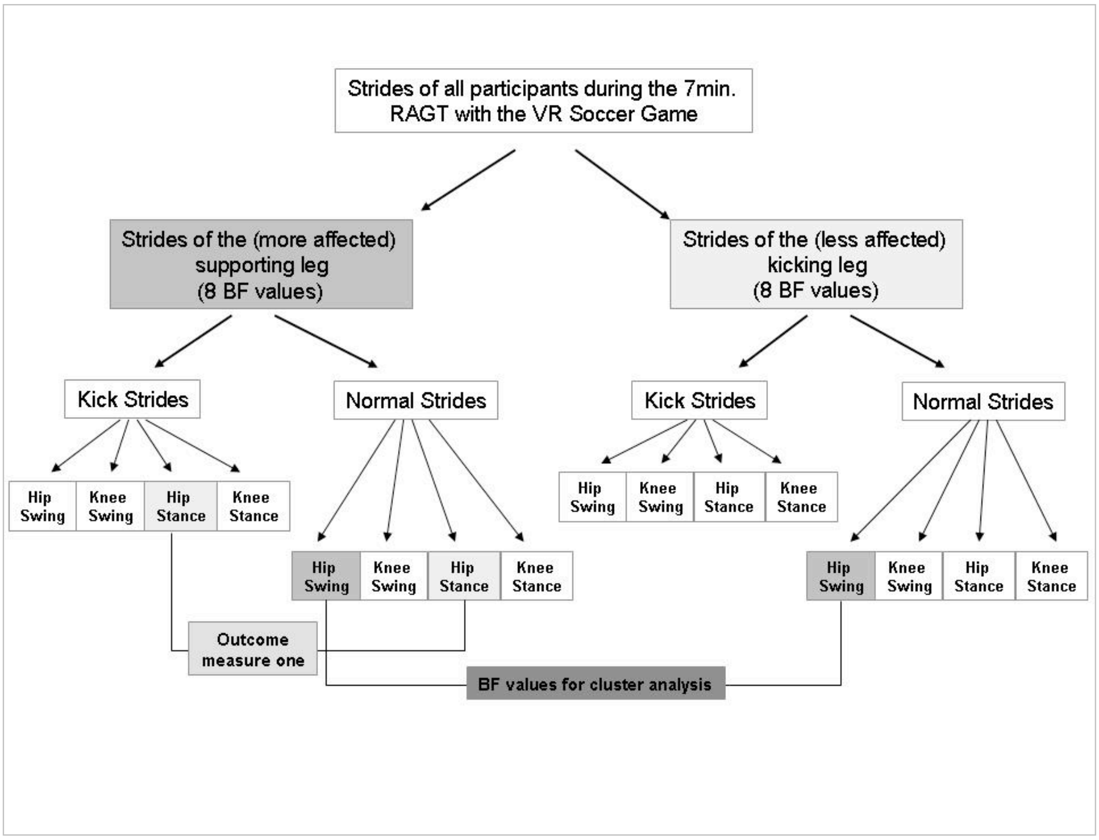

FIGURE 21: OVERVIEW OF THE ANALYSIS OF BF VALUES, SEPARATED IN STEPS FOR THE SUPPORTING AND THE KICKING LEG, RESPECTIVELY.

Comparisons in BF values during the kicking movement were made between (i) the healthy children and those with neurological gait disorders, and (ii) between children in the "high activity" and "low activity" groups. Additionally, differences in the position of the stance foot at the time of initial contact on the treadmill during the kick steps compared with normal steps were evaluated.

As the assumption for normally distributed data was not met, nonparametric Mann-Whitney-U-Test were performed for pair-wise comparisons between the groups (healthy children versus patients and high activity versus low activity pattern, respectively). For the pair-wise within-group comparison between BF values in kick steps and normal steps of the supporting leg the Wilcoxon test was applied. All statistical analyses were performed using SPSS 16.0.1 for windows.

6.4.4 Results

6.4.4.1 Healthy Children Versus Children With Neurological Gait Disorders

Age ($p = 0.28$), body height ($p = 0.81$) and bodyweight ($p = 0.67$) did not differ between the groups (two-sample t-test). Similarly, no differences were observed for sex ($p = 1.0$), the application of Lokomat® legs ($p = 0.21$; Fisher's exact test). Demographic characteristics are given in Table 1.

In the healthy children (Figure 22A), the BF values were significant smaller during kicking steps (mean ± SD: 26.57 ± 16.98) compared to normal steps (42.33 ± 21.17; $p < 0.001$). The patient group (Figure 22A) showed no difference between BF values obtained during kick steps (21.96 ± 22.93) compared to normal steps (24.37 ± 17.06; $p = 0.85$). The difference in BF values between normal and kick steps was significantly larger in healthy children than in patients (Figure 22C: $Z = -2.05$, $p = 0.04$).

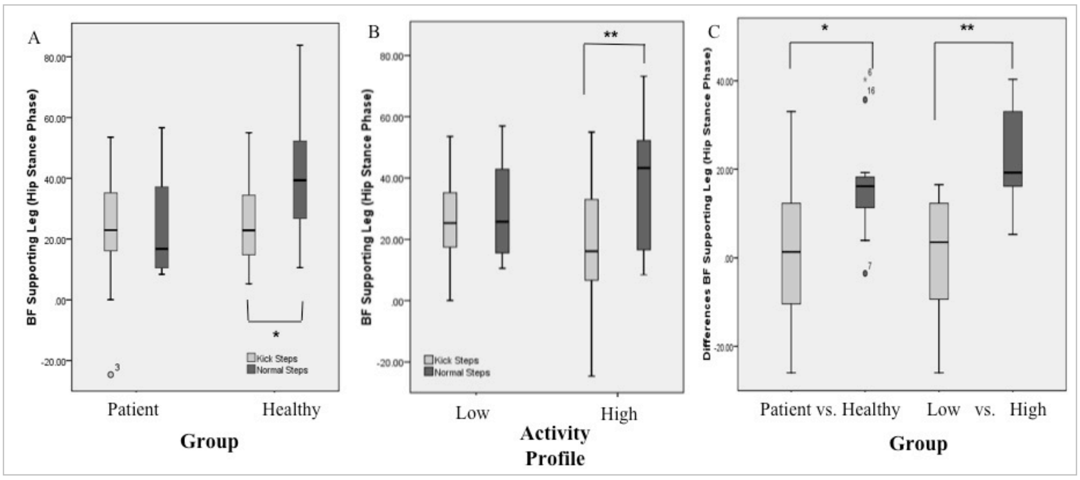

FIGURE 22: ABSOLUTE BIOFEEDBACK (BF) VALUES OF KICK STEPS AND NORMAL STEPS DURING STANCE PHASE, FOR (A) HEALTHY CHILDREN (N=13) AND PATIENTS WITH NEUROLOGICAL GAIT DISORDERS (N=10) AND, (B) CHILDREN WITH LOW (N=14) AND HIGH ACTIVITY PROFILES (N=9). (C) DIFFERENCE IN BF VALUES BETWEEN KICK AND NORMAL STEPS OF THE SUPPORTING LEG IN PATIENTS VERSUS HEALTHY CONTROLS AND IN THE LOW VERSUS HIGH ACTIVITY GROUP. POSITIVE VALUES INDICATE THAT THE BF VALUES WERE LOWER IN KICK STEPS COMPARED TO NORMAL STEPS (* $p < 0.05$, ** $p < 0.01$).

Healthy children (Figure 22A) positioned their stance foot significantly further in front during the kick steps (22.31cm ± 2.58) compared to normal steps (21.82cm ± 2.38; $p < 0.001$), whereas patients showed no difference in the stance foot position during kick steps compared with normal steps ($Z = -0.66$, $p = 0.56$). The difference in stance foot position between normal and kick steps was significantly larger in healthy children compared to the young patients (Figure 23C: $Z=-2.54$; $p = 0.01$).

6.4.4.2 Children With Low Activity Profiles Compared to Children With High Activity Profiles

Cluster analysis defined two clusters with distinct activity profiles obtained during the swing phase in all participants. The low activity group consisted of 8 patients and 6 healthy children whereas the high activity group consisted of 2 patients and 7 healthy children (Table 10). In the low activity group, the mean BF value was 9.80 ± 12.34 in the hip swing phase. In the high activity group, this value amounted to 46.04 ± 21.85.

TABLE 10: SUMMARY OF PARTICIPANT'S CHARACTERISTICS IN DEPENDENCE OF THE ACTIVITY

	Low Activity (n=14)	**High Activity (n=9)**	**p* (sig. 2-tailed)**
Group (Patients/Healthy)	8/6	2/7	0.197 [a)]
Sex (F/M)	3/11	7/2	**0.013** [a)]
Age (years) mean ± SD	11.0 ± 2.1	13.5 ± 2.1	**0.01** [b)]
Height (cm) mean ± SD	145.4 ± 11.6	159.4 ± 11.1	**0.009** [b)]
Weight (kg) mean ± SD	37.9 ± 11.0	51.9 ± 10.9	**0.007** [b)]
Lokomat® legs (kids/teens)	9/5	2/7	0.089 [a)]

[a)]Non-parametric test (Fisher's exact test); [b)]Two-sample t-test; bold=significant differences

Similar findings were observed as compared to the previous analyses. In participants with a low activity profile (Figure 22B), no differences in BF values were observed between kick steps (28.53 ± 15.35) versus normal steps (29.84 ± 15.22; $Z = -0.53$, $p = 0.63$). Participants with a high activity profile (Figure 22B) showed significantly smaller BF values for kick steps (18.40 ± 24.21) compared to normal steps (41.81 ± 27.45; Z = -

2.67, p = 0.004) and these differences were larger compared to the differences in the low activity profile group (Figure 22C: Z = -3.15; p = 0.001).

Similarly, participants with a high activity profile (Figure 23B) positioned their stance foot significantly further in front during the kick steps (24.37cm ± 2.74) compared with normal steps (23.77cm ± 2.49; Z = -2.67, p = 0.004) whereas children in the low activity group (Figure 23B) showed no difference in the stance foot position during kick steps compared with normal steps (Z = -0.16, p = 0.90). Again, the differences were significantly larger for the high activity group (Figure 23C: Z = -3.15; p = 0.001).

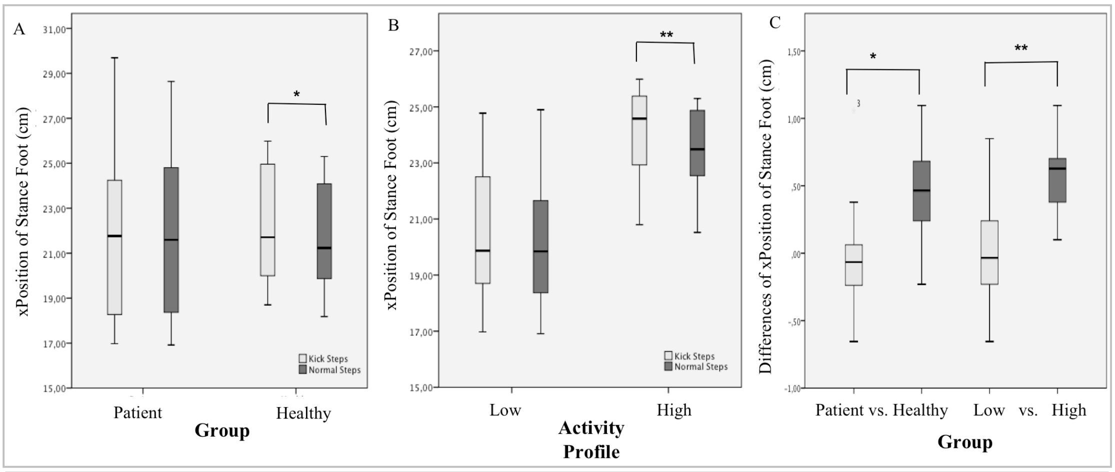

FIGURE 23: ABSOLUTE STANCE FOOT POSITION ON THE TREADMILL OF KICK STEPS AND NORMAL STEPS, FOR (A) HEALTHY CHILDREN AND PATIENTS WITH NEUROLOGICAL GAIT DISORDERS AND, (B) FOR CHILDREN WITH LOW AND HIGH ACTIVITY PROFILES. (C) DIFFERENCES IN STANCE FOOT POSITION BETWEEN KICK STEPS AND NORMAL STEPS IN PATIENTS VERSUS HEALTHY CONTROLS AND IN THE LOW VERSUS HIGH ACTIVITY GROUP (* P < 0.05, ** P < 0.01).

6.4.5 Discussion

The primary purpose of this study was to investigate changes in stance phase activity of the supporting leg performing a soccer kick during a VR-based RAGT in children with neurological gait disorders and age-matched healthy controls. A reduction in BF values should reflect that the participants took over weight bearing capacity of the supporting leg during RAGT. Furthermore, prolonged stance duration was inferred from a more frontal position of the foot during initial contact. A longer stride length in kick steps indicated that the participants tried to stabilize their supporting leg and put the center of gravity onto the supporting leg. On the one hand this pattern is similar to a football kick in real life, where the supporting leg takes over the bodyweight and lengthened the last stride for stabilization[118] and on the other hand, our findings are supported from an aquatic treadmill walking training in people post stroke, where an additional weights to the affected leg resulted in improved stability of the stance phase and gait symmetry[120]. Thus, our hypothesis that it would be possible to train the supporting leg during a VR soccer game was generally supported. However, these effects were mainly observed for healthy children or children in the high activity group.

6.4.5.1 Healthy Children Versus Children with Neurological Gait Disorders

Healthy children from a soccer club showed reduced BF values during kick steps compared to normal steps, whereas patients did not. Apparently, patients had difficulty in taking over weight with their more affected leg during RAGT, which can be explained by a reduction in muscle force in most of the patients and poorer leg muscle coordination. This is in line with other studies that investigated BF values during the swing phase (where higher BF values were indicative of better performance), and where lower BF values were found in patients compared to healthy children[116].

6.4.5.2 Children With High Activity Profiles Compared to Children With Low Activity Profiles

Similar findings were observed when participants with high and low activity profiles were compared. Interestingly, only two patients (number 2 and 10 in Table 1) were identified as having a high activity profile, whereas eight patients were allocated to the low activity group. Compared to the other patients, these two patients were relatively large, needed little to none assistive devices for walking (indicative of good leg muscle strength and control) and their diagnosis implied little cognitive impairment.

Overall, we could show that it is possible to influence stance phase activity of the supporting leg during RAGT, which has never been shown before. This finding has some clinical implications. First, only the least impaired patients in our study were able to correctly induce large leg activations and were able to take over weight bearing capacity on their supporting leg. It appears therefore to be a rather difficult task and not all patients will be able to train weight-bearing capacity during RAGT. Second, patients should participate actively during RAGT to be able to influence stance phase activity and efforts should be taken to avoid passive training situations by verbal encouragement of therapists or VR scenarios[107, 115, 116]. Third, these findings might be relevant especially for patients with asymmetric gait patterns as seen after for example congenital or acquired hemiplegia.

6.4.5.3 Study Limitations

This study has some potential shortcomings. Although, healthy controls and patients did not significantly differ from each other in demographic characterizations, the patient group was relatively small and heterogeneous in respect to age and diagnosis. Even though this reflects a normal pediatric rehabilitative population, it would be interesting to create a characteristic profile of patients which may benefit the most from this combined VR-based RAGT intervention.

The present study only investigated the reactions of patients with neurological gait disorders and healthy controls to stance phase activity in this VR game during a single training session. Clearly, the long-term effects of this VR game on stance phase activity and more important functional walking-related outcomes are very essential and should be investigated in future work. However, verifying the intended, presumably beneficial effects in a single training session was a necessary first step.

Finally, although two distinct clusters for the activity level were found, several demographic and biomechanical factors have to be taken into consideration to affect BF values, such as for example age, height, weight, unloading of bodyweight support, walking speed and type of Lokomat® legs as discussed above. In the present study these variables were standardized as much as possible, however, all those variables might influence each other.

6.4.5.4 Conclusion

Besides the positive effect of enhancing motivation with VR, as shown in previous publications, the present study showed an additional advantage of the VR soccer game during RAGT: Children with good leg strength and coordination were kicking with their less impaired leg, while the contra lateral leg was concurrently enhanced. Thus, training of the more affected half of the body in patients with neurological gait disorders during a VR-based RAGT is playfully possible without being consciously confronted with the impairment.

7 General Discussion

The purpose of this thesis has been to evaluate VR-based games for pediatric gait rehabilitation with regard to participant motivation and participation in patients with neurological disorders. This project was largely motivated by the need to develop engaging VR-based scenarios which have the capability to create a more appropriate rehabilitation environment for children. The three experimental studies involved addressed several questions. The first study explored various supportive conditions in order to gain knowledge concerning children's level of participation while walking on the Lokomat. The second study compared different VR scenarios with other supportive conditions and extended the first study with comparisons of longer conditions. The third study, focused on changes in stance phase activity during a VR soccer kick during RAGT. The findings of each individual study have been discussed in the specific discussion sections. In the following, the findings are first briefly summarized and discussed in conjunction with one another in the context of the respective research question as stated in the aims and significances of the thesis. Concluding remarks point out potential shortcomings of the study, discuss implications and provide suggestions for future research.

7.1 Summary of the Results

Both, therapists and clinicians are particularly interested to assess participation during RAGT and it is their goal to find the most effective and most strongly motivational interventions in pediatric rehabilitation. Results of the experimental studies were promising. The first study investigated differences in therapy conditions on a single day and compared active participation during a short time period (two minutes). Within this period we showed that VR has the same immediate effect on motor output as therapist supportive instructions in children with neurological disorders. Most importantly, this study revealed that both patients and healthy children achieved significantly higher motor output during all supportive conditions as compared to walking without any motivational assistance. In other words, active participation was increased either by verbal encouragement given by a physical therapist, by a VR soccer scenario or by the combination of both VR and therapist. It is not yet known whether such enhanced active performance can also be maintained over longer time periods or during a whole training session and whether this leads to a more effective rehabilitation process for patients. Therefore, the second study aimed to compared different VR scenarios (soccer game and navigation game) with other supportive conditions over longer periods of time. Results of this study showed that both VR-based therapy forms were equally the most effective in inducing the desired response in the patients and healthy controls with regard to active participation during a seven-minute training period. Thus, we were able to extend the findings of the first study by showing that RAGT coupled with VR can either improve active participation in children and maintenance over longer time periods compared to other supportive conditions. In particular, both VR conditions resulted in higher participation compared to normally applied support such as therapist instructions or watching a DVD, in both patients and healthy children. The third study assessed whether it is possible to train concurrently the supporting leg while concentrating on the kick during a VR soccer game. The purpose of the study was to explore the changes in the stance phase activity during VR kick versus normal steps. Since patients tend to use their healthy leg favorably for a soccer kick during the VR-game, this study hoped to show that the contra lateral leg was subconsciously trained at the same time.

7.2 Motivation in Pediatric Rehabilitation

This thesis was largely motivated by the need to develop engaging VR-based scenarios for children which allows therapies to be applied on consecutive days for about 30 minutes over 3-5 weeks without boring routine. As outlined in the theory section, patient motivation plays a crucial role in determining therapy outcome, especially in the field of pediatric rehabilitation. Motivation is usually not a constant factor but rather a dynamic process which is dependent on many internal and external factors. Gaining awareness of the factors which may decrease motivation during rehabilitation will also foster a better understanding of the phenomenon of patient disengagement during rehabilitation[78]. In particular, active engagement towards a training intervention is usually equated with motivation; passivity with the lack of motivation[108].

Findings of VR studies in children with CP have indicated that immersion in VR allows children to participate in activities which are within their physical capability, thus, creating an increased feeling of self-efficacy and a sense of control compared to that of patients in pre-test patient reports[93, 109].

It should be pointed out that the social interaction between therapists and participants undoubtedly plays a crucial role, especially for patients. Thus, the use of VR during rehabilitation therapy should not replace the physical therapist, but rather provide an additional means of enhancing training efficiency and motivation. The flexibility of VR will allow therapists to tailor VR systems to the development and cognitive constraints of the diverse group of patients with neurological disorders. Furthermore, VR is able to cope with aspects of age, gender and disorders in clinical populations. Thus, such critical aspects and circumstances should be a central focus of further studies in order to obtain the most promising motor outcomes and optimal conditions for therapy. In any event, motivation may be regarded as a booster during pediatric rehabilitation.

7.3 Feedback and Motor Learning

It has been proposed that active training is more effective than passive training for motor learning and cortical reorganization[63]. Important findings in stroke patients suggest that simply moving or passively exercising the impaired limb does not lead to maximum recovery. Furthermore, it has become apparent that new motor skills, enriched and task-oriented practice environments and primarily motivating tasks which increase engagement are necessary for motor (re)learning and recovery after stroke[90]. Although, there are substantial differences in motor learning in children with CP and those having experienced stroke or spinal cord injury, in cases in which the patients did have an intact and normally functioning nervous system prior to injury, it has been shown that activity, task-specificity and goal-orientation are also crucial aspects in treatment of children with CP[99, 100]. Therefore, in RAGT it is essential that patients participate actively instead of just letting themselves "be walked". Motor learning can also be driven by feedback. With the advanced biofeedback facility integrated in the Lokomat system used, we were able to record force interaction between the patient and the Lokomat and, on the basis of this data, to estimate the participants' performance. Hence, the findings of this dissertation demonstrated that the feedback given by VR-based training conditions had a positive impact on motivation and active participation in children with and without neurological disorders.

7.4 Limitations

Despite initial promising results in the field of VR-based RAGT in terms of feasibility in pediatric rehabilitation therapy and the desired effects in active participation, we are aware of potential shortcomings in these studies. First, all three studies investigated differences in therapy conditions on a single day and for two different short time periods of two and seven minutes. We have chosen this methodological design due to the comparability of the biofeedback value. Indeed, the biofeedback values are not only influenced by the walking performance of the participant, but also by other factors such as slightly altered attachment of the exoskeleton, body-weight support, treadmill speed and synchronization of the exoskeleton and the treadmill[80]. Since the influence of these factors was often unknown as well as difficult to predict, we decided to hold as many factors as possible constant and not make any adjustments between the different conditions. Thus, the time period of the second study was the longest possible duration for investigating differences in several conditions within one therapy session of 45 minute. Furthermore, patients were heterogeneous with respect to age and diagnosis. However, this reflects a normal pediatric neurorehabilitation clinic population, and the healthy control group was matched for age and gender. Another limiting factor might be the safety system of the Lokomat. The device has built-in force monitoring which stops the robotic drives if the participants provide too much force input. These technical limitations influenced the measurements, primarily those of the healthy children. Healthy children understandably have more power than patients, and therefore occasionally activated the safety mechanism. Hence, some conditions may be slightly underestimated in terms of motor output values. On several occasions during measurement, the force exerted in the VR and VR plus therapist's conditions and triggered the Lokomat's safety mechanism. This led to frustration, which in turn caused the healthy children to reduce their force and therefore produce lower motor output values than would otherwise have been possible and expected during the affected conditions. Finally, the two VR game scenarios used in this work have some restraints. Despite the continuous enhancements of the implemented VR scenarios during the past three years, the games only provide suspense for about 15 minutes after which the children lost interest in the game. Therefore, emphasis should be placed on the development of engaging and immersive game designs.

7.5 Conclusion

The present thesis and the investigations of the three studies contribute to the corpus of the field of studies in the field of VR-based gait rehabilitation. The results broaden our knowledge regarding participation and motivation in children during training on the

Lokomat coupling the well-established Lokomat with new VR technologies should provide more interesting and more motivating therapy sessions. Furthermore, man-machine interaction forces (biofeedback values) measured during the Lokomat training provide specific motor feedback for both therapists and patients, which in turn has been shown to be a crucial factor in motor learning.

Overall, the experimental studies in this thesis were only possible due to the collaborative efforts among a team of clinicians, engineers, game designers and neuroscientists.

8 Implications for Future Work

The present thesis extended the current work of VR-based gait rehabilitation regarding the feasibility of VR-based Lokomat training and the desired promising results which have demonstrated that patients with neurological gait disorders and healthy children were motivated and participated more actively with VR-based conditions than with other interventions. As these findings suggest, VR rehabilitation in children appears to be a promising field and new questions have arisen from this work. As already mentioned, further research should target the development of new engaging and immersive VR games which allow target specific rehabilitation trainings and different performance levels. Furthermore, cognitive and spatial aspects could be implemented in serious game designs in order to increase their therapeutical value. In future research, it might be of interest to consider different cognitive levels in patient population as this might have impact on rehabilitation outcome.

One interesting question is whether or not the expected behaviors or actions measured within VR rehabilitation can be expected to be transferable to real world functions. Mainly, VR-based therapy offers physically disabled children an opportunity to be active and independent while engaging in activities (e.g. VR soccer game) otherwise too difficult for them and to perform training in a safe environment which resembles real life[67, 68]. Therefore, in order to accomplish effective training, it is necessary to test transferability of practice to real world performance[66].

Another open question is whether VR-based RAGT strategies maximize the therapeutic outcome in terms of reduced therapy duration and an improved gait quality. However, this kind of research requires visionary and thoughtful game designs, and these have yet to be developed. Yet another reason for developing new games is that in the field of pediatric rehabilitation, we were faced with the problem of holding children's attention during consecutive training sessions. Therefore, interactive game techniques are needed in order to promote participation and compliance, which allows children to train different gait pattern while fully focused and immersed in virtual environments.

Due to the great need for new VR-based games, we have recently initiated another cooperative project with the Department of Game Design at the "Zürcher Hochschule der Künste", ZHdK Zurich. The purpose of this interesting collaboration is to improve the quality of VR design elements and immersion according to game design principles[121]. Hence, we expect in future research that evaluation of these new games will reveal further improvements in aspects of motivation, participation and functional rehabilitation.

9 References

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10 Curriculum Vitae

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10/2002 - 07/2006 Institute of Psychology, University Zurich
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04/2008 – 03/2009	Olga-Mayenfisch Stiftung

PUBLICATIONS

PEER-REVIEWED

Birrer-Brütsch, K., Mansouri, S., Duschau-Wicke, A., Jäncke, L., Grüneberg, C., Meyer-Heim, A., van Hedel, H.J.A. Influencing Stance Phase Activity in Children During a Virtual Reality Based Robot-Assisted Gait Training (submitted manuscript).

Hänggi, J., Brütsch, K., Siegel, A.M., Jäncke, L. The Architecture of the Chess Player's Brain. (submitted manuscript).

Brütsch, K., König, A., Zimmerli, L., Mérillat(-Köneke), S., Riener, R., Jäncke, L., Meyer-Heim, A. (2011). Virtual reality for Enhancement of Robot-Assisted Gait Training in Children with Central Gait Disorders. J Rehabil Med. 43, 6: 493-9.

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INVITED REVIEW

Brütsch, K., (2010). Virtual reality for robot-assisted gait training in children. CyberTherapy & Rehabilitation 3: 30-31.